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THE BIOPHILOSOPHICAL SIGNIFICANCE OF ARTIFICIAL HIBERNATION *Félix Martí Ibáñez*

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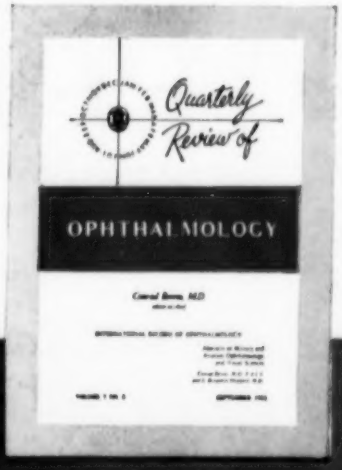

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1. Freed, S. C.: Internat. Rec. Med. 166:465 (Nov.) 1953.
2. Rees, L.: J. Ment. Sc. 99:62 (Jan.) 1953. 3. Morton, J. H., et al.: Am. J. Obst. & Gynec. 65:1182 (June) 1953.
4. Morton, J. H.: Internat. Rec. Med. 166:505 (Nov.) 1953.

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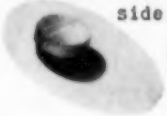

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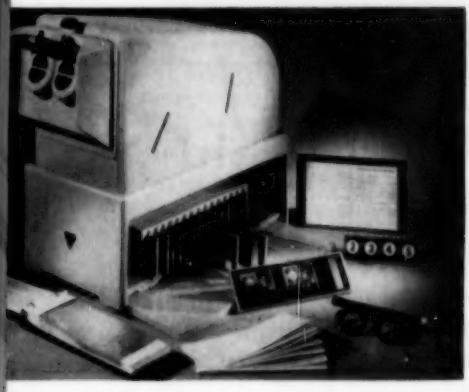

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RECORD OF MEDICINE
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The Biophilosophical Significance of Artificial Hibernation

Félix Martí-Ibáñez, M.D.
NEW YORK, N.Y.

Through the gateway of his concept of artificial hibernation, Dr. Henry Laborit ushers us into that vast dark-roomed palace which is the physiopathology of the neurovegetative system. Ghostly shadows fill this area of neuroendocrine pathology where proved scientific facts exist side by side with new theories. But Dr. Laborit walks ahead of us, opening windows and turning on the lights, erasing shadows and illuminating theories as new in their meaning as they are traditional in their empiricism. For artificial hibernation, to which we are devoting a symposium in this issue of the INTERNATIONAL RECORD OF MEDICINE, is not merely a new therapy but rather a widening of the horizon of Modern Medicine; it is based on a medical philosophy that promises to revolutionize classic concepts hitherto considered immutable. Let us reserve for the brilliant contributors to this symposium the task of explaining the technics, applications, and possibilities of artificial hibernation. Our purpose here is to stand on the threshold of that vast and shadowy dominion, illuminated by the clinical experiments of Laborit and his collaborators, and sketch a blueprint for those unfamiliar with this therapeutic system.

Biology teaches us that man, like many animals, is a homeothermic being, capable of maintaining the stability of his inner milieu—intercellular fluids, vascular lymph, and blood—and the constancy of his body temperature through the functioning of thermoregulating physical and chemical mechanisms. Because of these mechanisms, man is a warm-blooded animal in contrast with the cold-blooded animals called poikilotherms, like the lizard, whose body temperature is on a par with that of their environment. As Claude Bernard demonstrated, the stability of the inner milieu permits us to enjoy an independent life, safe from environmental variations.

The biological instrument used by our body to guarantee the constancy of its temperature and the stability of our inner milieu is the neurovegetative system—and

certain mysterious areas of the nervous system, like the thalamus and hypothalamus—whose vast network is integrated into the endocrine glands, thus forming a neurovegetative-endocrine system, without which man would not be able to enjoy biological freedom and his life would be at the mercy of any change in external temperature. Because of this system, the body of an Eskimo in icy Lapland and that of a Zulu in the burning heart of Africa have the same temperature. Many years after Claude Bernard established this basic concept of modern physiology, Walter Cannon baptized it *homeostasis*, and from then on it has been considered the ineluctable condition of independent life and the most precious physiological gift enjoyed by man.

Several years ago, in the wake of the new concepts introduced by Reilly and Selye, who established the consequences of that powerful, unspecific external aggression called *stress* upon the human being, it was observed that the reactional capacity of the human body to external aggressions could be so violent that it could cause a state of shock frequently resulting in death. The mechanism of this biological catastrophe is the overreaction of the organism to aggression from the environment; the body violently mobilizes a series of drastic defensive reactions whose purpose is the maintenance of the termic autonomy of the organism, that is, its homeostasis. These reactions can be so intense that they exhaust the individual. The mobilization of his defenses to resist the onslaught of an external aggression frequently produces a collapse of the organic fortress, as if the suddenness and magnitude of the defense measures were even more harmful to the fortress than the possible attack from without.

The neurovegetative system, the hypothalamus, and the endocrine glands are the causes of these reactions, which can consume the last bit of organic energy and produce a sudden drop in blood pressure, a reduction in the volume of circulating blood, shivering, and other symptoms characterizing shock. This occurs because our organism attempts to defend itself against an aggression that is greater than its means of defense. Shock is a typical example of the fact that—contrary to the claims of classical medicine—not all physiological reactions are beneficial, and it also is a further confirmation that pathology and physiology make up one area in which frontiers are arbitrarily defined.

Our neurovegetative system is capable of defending our lives under normal or moderately abnormal conditions, but when it is faced with aggressions of exceptional gravity, it exhausts and kills us. As the classical proverb has it: "The cure is worse than the disease." In such cases, the attempt of the neurovegetative system to maintain the stability of our inner milieu may be made at the price of our lives.

When Laborit began his search for a means of combating shock reactions, he was guided by the desire to solve a problem common to all physicians of all times. In the course of his reading he had come across old reports of physicians at the Val de Grace Hospital who had taken care of soldiers wounded while fighting under the Napoleonic banner; these reports stated that the patients had survived tremendous ordeals and that they had come through under very low temperatures. Such claims dovetailed with others made a century before Napoleon by French explorers who had survived similar privations, wounds, and other sufferings in the frozen waste lands of Canada. But Laborit also read more recent books and was drawn to the work of

Finnish and American scientists on the production of experimental hypothermy in animals. All this led him to suspect that blind acceptance of the principles of Claude Bernard might entail risks, and, after studying Reilly and Selye, he began to wonder whether one should base the solution to the problem of shock not so much on man's capacity to resist unusually intense external aggressions as on his ability to adapt himself to them—to yield to them temporarily without any struggle. If we may be permitted the use of a pugilistic term, in such cases it might be more useful to "roll with the punch," like the boxer who deadens his opponent's blow by letting his body be carried away by the strength of the punch rather than receiving the impact of meeting it full-on.

As a backdrop to the work of Laborit and his school, there existed a very rich folklore and a vast treasure of empirical "know-how" among countryfolk. If one could temporarily reduce the vitality of the human being without causing any lesion, it might perhaps be feasible to let a physical agent play a very important part in vegetable and animal biology. If Nature teaches us that excessive cold is the mortal enemy of living beings, it also shows us, paradoxically, that that extreme cold may insure survival. Horticulturists know that the best time to transplant plants and even trees is in mid-winter, and the colder the better, for then the plants and trees are not traumatized. Marmots and other hibernating animals live all winter *au ralenti*, and their organisms suffer no lesion.

Jentzer, of Geneva, found many living trout frozen in blocks of ice in a lake in Gothard. Taking them in his hands and observing that they were as stiff as wood, he traumatized them in every way with sufficient intensity to kill a living trout several times over. However, when he returned them to frozen water, which was then warmed, the trout revived without having suffered from the traumatisms in any way. This means that poikilotherm animals, like insects, lizards, and batrachians, resist, without defending themselves, aggressions from without (especially cold) simply by adapting their temperature to that of the environment. Such a phenomenon is possible, according to Jentzer, because those animals do not have a neurovegetative system. But the human being has a neurovegetative system that is more highly developed than in any other species and which sets in motion against any *external* (thermic, surgical, physical, etc.) or *internal* (chemical, medical, etc.) aggression a series of reactions in the nature of a neuroendocrine defense of homeostasis; these reactions frequently are beneficial but in cases of unusual aggressions may exhaust and even kill the organism. As a name for "this dragon" of excess threatening "the Saint George" of homeostasis—to use Cannon's picturesque image—Dickinson W. Richards recently suggested *hyperexis*, a Greek noun meaning a reactional excess and first used two thousand years ago in the dialogue *Timaeus* written by a splendid Athenian called Plato.

The refrigeration of the body as a means of lowering defense reactions is a revolutionary measure. For centuries the obsession of the physician has been "to increase organic defenses" as a means of preserving the constancy of the inner milieu and fortifying it against pathological or traumatic aggressions. Therefore, the idea of refrigerating the body to enable it to adapt itself *passively* to the aggression instead of fighting it represents a reordering of classic physiology from the ground floor up.

The effect of hypothermy of the body is to reduce the organic requirements and consumption of oxygen, to lower metabolism, and, with the reduction of capillary circulation and loss of radiating heat, to decrease the burning flame of metabolism and cellular oxydation to the strength of a tiny flickering light. This obviously would bring about notable advantages in brain and heart surgery when attempt is made to interrupt the flow of blood to our vital organs. For some time now physicians have had recourse to *refrigeration* of a part of the body as well as of *hypothermy* or refrigeration of the *entire* body with a lowering of its temperature to 25°C. or even lower (deep hypothermy). This method was employed by Bell as far back as 1812 to treat pain and by Arnott 103 years ago to treat carcinoma. The term "artificial hibernation" was originally employed by Simpson in 1905 and revived in 1951 by Laborit and Huguenard, who were the first to strengthen anesthesia by means of certain drugs and then to provoke a neurovegetative block accompanied by induced hypothermy. The term artificial hibernation therefore should not be applied to the method as such but to the state of autonomic block and reduction of body vitality to the minimum.

In order to block the neurovegetative system and prevent it from liberating chemical substances, which, like a clarion call, mobilize organic defensive reactions, Laborit decided to experiment with substances that might provoke a "lysis" or interruption of the defensive mechanisms of the body, a *neuroplegia* or disconnection —on all possible levels—of the neurovegetative system and even of the central nervous system if possible. Laborit and Huguenard began to test different neuroplegic or lytic drugs by mixing various ingredients of diverse effects and ofttimes of unknown total results, but which produced a certain "intoxication" followed by a twilight state that justifies the term *lytic cocktail* or *liberation cocktail* introduced in 1953 by Huguenard. In point of time, neuroplegia had been brought about prior to the work of these two scientists: e.g., the medicophilosophical systems described in Hindu yogas, the anoxi-anesthesia of Crile, the deep anesthesia of Bigelow, the muscular relaxants of Krogh, procain perfusions, high rachianesthesia with vagal cervical block, the sleep cures with local anesthesia of Vijnejkij, and the cortical blocks of Russian psychiatrists who were the forerunners in the use of neuroplegia in psychiatry as applied today in France by Delay and his collaborators.

What Laborit and his co-workers aimed at from the very beginning was to bring about an artificially induced hibernation in man, similar to that of hibernating mammals and cold-blooded animals. This means that hibernation is more than just inducing prolonged sleep. It entails calming the disorganized reactions of the neuroendocrine system at a given crucial moment and thus imitating the physiological attitudes of certain animals which are not as highly developed and free as man but are, on the other hand, less fragile. As Laborit has said, it is a matter of "temporarily abandoning a metabolical luxury with which we can no longer maintain life and adopting a more modest type of life, in order to await a return to a regime of free interexchange and more favorable conditions of life in the environment." Artificial hibernation thus becomes in cases of civil traumatisms or war wounds something more than a therapeutic technic: it becomes part of a treatment by which we can

survive, as has been shown in surgery, psychiatry, and especially in military medicine, which has saved innumerable lives.

The search for the royal road to artificial hibernation has led to the search for chemical compounds that might strengthen the effect of refrigeration of the human body brought about by iced sheets and other means which cannot cause dangerous bronchopulmonary reactions when such compounds have deprived the body of the ability of reacting against the cold. This combination of a *lytic cocktail* and refrigeration may revolutionize the treatment of shock. No longer may the defenses of the body be stimulated as hitherto by heating the body, applying stimulants, or administering tonic medications which sometimes cause an increase of organic reaction so out of proportion that the body, exhausted by its own natural reactions and the reaction induced by stimulants, succumbs like a worn-out horse whose rider has beaten it violently. Instead, the organic functions can be reduced to a minimum level bordering on the inertia of hibernating animals.

After several attempts Laborit decided to use a drug with a phenothizine base (phenothiazine) of strong lytic effect. Later there was obtained, as a derivative, chlorpromazine, which has one of the broadest known spectrums of activity on the nervous system, since it is at the same time sympatholytic, vagolytic, spasmolytic, and sedative. To this drug Laborit and Huguenard added two more (promethazine or phenergan, and pyridosal or pethidine) whose effects are primarily sympatholytic, adrenolytic and vagolytic, and secondarily hypnogenic (lobotomizant), analgesic, and mioresolutive, the *cocktail* being administered by intravenous perfusion drop by drop.

Thus, the combination of induced neuroplegia and refrigeration of the patient produces the state of artificial hibernation characterized by hypometabolism, hypothermia, hypotension, hyposecretions, and biological indifference of the organism to external aggressions. For the neuroendocrine system is stabilized and the rhythm of life is slowed down by pharmacodynamic mechanisms while the lytic cocktail "sends the adrenal-pituitary couple on a vacation," as Laborit has put it with typical Gallic humor.

When the organism is deprived of nutrition it draws on its own reserves of protides and lipides since the metabolism of the glucides is blocked. Laborit has recently started to use injections of somatotrophic pituitary hormone which favors protide anabolism and catabolizes lipides, like hibernating animals who, in winter, during their sleep, consume their fats but not their proteins or their sugars which they need when they wake up in the spring.

The cold of hibernation eliminates the antistress reaction (often very dangerous in states of shock) of the organism and protects it from the aggressor factor, at the same time lessening, by its narcobiotic action, microbe pullulation and toxic reabsorptions. And so, of the two factors necessary for the development of a disease—the pathological aggressor factor (traumatism, microbe or toxin) and the reaction of the attacked organism to the same—the second factor is eliminated, thus protecting homeothermic life at the cost of putting conscious life to sleep, sheltering the organism from the threats of stress whether it be traumatic, toxic, infectious, or

even emotional and psychiatric in type. And all this, thanks to the chemically induced "vacation" of the neurovegetative–endocrine–hypothalamic system.

From the aforesaid we can see that artificial hibernation is as ancient as Nature itself and imitates the method Nature has given trees, plants, fish, reptiles, and many other animals for defending themselves from bitter winters and the attendant lack of food. Prehistoric man must have possessed this quality to a certain degree, but lost it as he learned to defend himself consciously from cold and hunger. Animals still use this recourse of sleeping away long months of cold and hunger. Their breathing slows down as well as their pulse, their temperature falls, their consumption of oxygen decreases to a minimum, organic elimination is interrupted, and the neurovegetative block and coma of certain sensorial areas of the brain eliminate external sensations which, like the cold, would make them awaken and consume too much energy. Instead they feed on small amounts of fat stored up in the organic pantry of their own body. These fats are consumed and burned up slowly so that they will last until the animal awakens.

Man has done nothing more than scientificially imitate the mechanism of natural defense used by animals. Lecomte de Nouy (quoted by Jentzer) has said: "The criterion of adaptation is usefulness, while the criterion of evolution is freedom." The error of early research and conclusions was to mistake evolutive features for vital phenomena. Instead of exalting means of defense—which often accelerate exhaustion of the cells, thus precipitating death—the new artificial hibernation causes us to lose our freedom temporarily through neurovegetative blocking of harmful reactions; and during the period of repose and sleep, the hibernated organism has time to recover and save its life.

Laborit and his collaborators have led us into a vast mansion of mysterious shadows—artificial hibernation—and have revealed some of its treasure rooms which will be explored by legions of investigators the world over. We stand on the threshold of a new era of research into vegetative and endocrine phenomena and perhaps also into new psychiatric methods and a widening of our knowledge of biology and human pathology. Artificial hibernation does not correct Claude Bernard; it broadens the horizon he described and provides a new theory and promising tools for the research biologist so that he may constantly progress towards that ideal of happiness —unattainable in Medicine—enjoyed by the man who knows the causes of things. Virgil expressed it in one line: *Felix qui potuit rerum cognoscere causas.*

SYMPOSIUM ON ARTIFICIAL HIBERNATION

Guest Editor—HENRI LABORIT, M.D.*

Potentiated Anesthesia

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The term "potentiated anesthesia" is proposed to define a type of anesthesia which has been described elsewhere in these terms:

"The organism to be anesthetized is placed, by means of drugs, which themselves possess little or no anesthetic properties, in a condition where weak anesthetics, in doses generally insufficient to induce the profound narcosis required by major surgery, will nevertheless produce a constantly effective general anesthesia."[1]

While this definition remains unchanged, new pharmacodynamic agents have since appeared inasmuch as research and organic synthesis were from then on oriented towards the potentiation of general anesthetics. It should be noted that, as a surgeon, the author was primarily interested in discovering an organic protection against various types of aggression. Our incursion into the domain of anesthesia was in a sense accidental; this is confirmed by the fact that our methods have been extended beyond the limited field of anesthesia to that of general pathology.

PHYSIOBIOLOGIC BASES

The obscure phenomena of general anesthesia may be studied under the two general headings of peripheral and central mechanisms.

(A) *Central biologic phenomena.* These apparently consist of an enzymatic blockage of cerebral metabolism, which is essentially that of carbohydrates. It so happens that the derivatives of phenothiazine (the major elements in potentialized anesthesia) appear to inhibit carbohydrate metabolism. This theory is supported by the following data: frequent hyperglycemia in animals undergoing artificial hibernation, which is not explained either by glycogenlysis or by neoglycogenesis;[2] a constant reduction in the respiratory quotient that may be explained in other ways, but which takes on a certain significance when correlated with parallel ideas; the fact that in prolonged deep hibernation, experimental animals lose more weight than the controls whose total metabolism is nevertheless much higher, indicating that the latter are using up materials lower in energy than carbohydrates.

It appears probable that, from the biologic standpoint, these phenothiazine derivatives interfere with the function of the central nervous system by inhibiting a stage

* A short biography of Dr. Henri Laborit appears on page 360.

in the catabolism of carbohydrates. Peruzzi and Forni were able to show that one potentiating agent, 4560 R.P.,* reduced cerebral metabolism without affecting either renal or hepatic metabolism. The inhibition of carbohydrate catabolism at the cerebral level might therefore be one of the causes of potentiated anesthesia.

(B) *Central physiologic phenomena.* In 1951 I suggested that the action of certain drugs on the central nervous system would affect interneural connections between the cortex and the diencephalon.[1] This action was clarified recently by the work of Terzian[2] and of Dell, who showed that 4560 R.P. acts on reticular tissue, i.e., on the associative cells which play such an important part in insuring a relay between the branches from the peripheral sensory region and the cortex, on the one hand, and between the centrifugal pathways, on the other.

(C) *Peripheral phenomena.* In my experiments and reports of 1951, I also emphasized that basal metabolism must be lowered in order to facilitate anesthesia. Although the drugs currently used produce a true basal metabolism in human beings by inducing a vegetative, endocrine, and affective relaxation, they do not appear to produce a hypometabolism when used singly and unaccompanied by hypothermia. This point was emphasized by the author and his colleagues in their first report on 4560 R.P.[4] The drugs certainly inhibit hypermetabolism as a secondary reaction to emotion and to surgical shock, but if thermolysis is controlled in man, the metabolic decrease induced by 4560 R.P. alone is negligible. The hypometabolism observed in small animals is caused by significant hypothermia following the law of Van T. Hoff, if the animal's environment permits it. This hypothermia itself results from a thermolysis increased by peripheral vasodilation in an animal whose body surface is large in relation to its active protoplasmic volume and whose thermoregulation is otherwise blocked. Thus, thermogenesis is unable to compensate for this increased caloric loss.

It is not at all certain, in my opinion, that the endocrine inhibition associated with the use of 4560 R.P. or of potentiated anesthesia can be correlated with the pharmacologic action of drugs, despite the results obtained by Jentzer, Bobbio, Castaigne, Aron et al, and Li Voti.[5, 6, 7, 8, 9] However, it is likely that hypothermia plays a large part in this endocrine relaxation.[10] It should be noted, however, that we already demonstrated the inhibition of the pituitary (a continued finding) by the sole action of the lytic mixture, as seen in the reduction of eosinophil cells[12] during and after surgery. Certain experiments indicate that elements in the lytic mixture exercise an adrenocorticotropic effect.

How should these divergent results be interpreted? Firstly, it should be noted that this corticoadrenal stimulation was established in the rat, a small animal in whom the injected mixture cannot operate as slowly and as progressively as in man. The peripheral vasomotor effects of the drugs thus exercise a brutal and "aggressive" effect which might explain the endocrine reaction, a reaction that might have been avoided by a slow and progressive pharmacologic effect.

We could also state that a stimulation of the endocrine system is followed by a secondary inhibition which blocks vasomotor reflection. These are merely hypoth-

* See list of drugs on page 320.

eses, but we believe that some drugs are capable of inhibiting hyperfunction resulting from shock without blocking the physiologic functions of the endocrine system. Marquardt[11] recently showed that 4560 R.P. strongly inhibited the response to epinephrine but only feebly affected the response to nor-epinephrine. Holtz interpreted this as an explanation of the maintenance of "minimum" function of the vegetative system and of the blockage of the "danger function." Directly or indirectly, the same effects appear to operate at the level of the endocrine glands. It may well be that when carbohydrate catabolism is inhibited, the pituitary no longer reacts to the chemical aggression of 4560 R.P.

While the hypometabolism induced by each of the drugs singly is negligible in man, the mixture of drugs is, on the contrary, strongly hypometabolizing because of the potentiation of drugs such as demerol (with a well-defined hypnogenic effect) and especially of the barbiturates whose action on cellular metabolism is known. For this reason, it is essential to distinguish clearly the action of the drug mixtures we recommend: (a) to facilitate anesthesia and (b) to protect the organism against various shocks, including surgery. The latter function is the more important of the two.

FACILITATED ANESTHESIA

The basic principle of potentiated anesthesia, as we stated it in 1951, is to use atoxic or low-toxicity drugs to place the organism in a state of "suspended animation," like the condition found in hibernating animals, so that only light doses of an anesthetic will be required to obtain narcosis; the anesthetic will then have been potentialized by various drugs.

Since the parasympathetic system appears in principle to regulate anabolism and control sleep, it seems logical to leave it unblocked and, on the contrary, to inhibit the adrenergic sympathetic fibers which enter into catabolism, into the organism's reaction to its environment, and into carbohydrate metabolism. Effectively, if we consider a slight vagal predominance desirable, it can only be the case in an organism that is already deeply blocked in both the adrenergic and the cholinergic directions.

Inhibition of the adrenergic system results in a spasm of the smooth muscles of the entire pulmonary tree; the danger which can ensue in anesthesia is evident. Hence, the need to obtain a balanced neurovegetative block while maintaining secondarily a discreet vagal predominance of the type observed in hibernating animals. Contrarily, in certain cases such as thoracic and pulmonary surgery, vagal blockage is desirable; some drugs such as diparcol—ganglioplegic and parasympatholytic—will be useful to produce bronchial dilatation, arrest secretion, and stimulate breathing. The anesthetist has at his disposal such ganglioplegic drugs as tetraethylammonium chloride, methonium salts, and procaine amide, which permit him in certain cases to produce a predominantly vasomotor inhibition and to obtain controlled hypotension by postural drainage.

Adrenolytic drugs such as 4560 R.P. and sympatholytics like hydergin are nearly always indispensable to block organic reaction to aggression and to facilitate anesthesia. Parasympatholytic drugs are of lesser importance, inasmuch as the presence

of demerol in the lytic mixture, with its powerful atropinic effect, and the vagolytic properties of synthetic antihistamines (particularly phenergan), as well as 4560 R.P., will in most cases be sufficient to block any muscarinic effects. If a stronger action is required, rather than use atropine, we prefer diparcol which combines a powerful ganglioplegic action with its atropinic properties.[14]

The antihistamines (phenergan) are undoubtedly useful for their effect in keeping closed the precapillary sphincters, thus effectively counteracting the histaminic effects of many drugs such as the curare group. We were particularly impressed by their action both centrally and on capillary permeability. As soon as the antihistamines were introduced into anesthetic and surgical therapy, we became interested in their hypnogenic, antithermal, and antiemetic action,[12] properties which were subsequently looked for in diparcol and developed in 4560 R.P.

Anesthesia is facilitated by the combined action of drugs on the peripheral vegetative system and on the centers, as we originally claimed and as the work of Dell with 4560 R.P. has confirmed. Dell effectively showed that section of the spinal bulb produces in the experimental animal cortical waves of sleep resulting from the interruption of the sensitivo-sensory paths, whereas normally the arrival along these paths of peripheral excitations maintains the waking state. When the sciatic nerve is irritated, however, the waves of the waking state are seen (evidence of the direct action of epinephrine), liberated in response to stress, on the brain.

The injection of 4560 R.P., without section of the spinal bulb, produces waves of physiologic sleep as the result of the drug's action on the reticula, namely a central action. But in this case, irritation of the sciatic nerve does not produce a waking rhythm, inasmuch as the drug is also adrenolytic and exercises a peripheral action. Thus, potentiated anesthesia effectively rests on the neuroplegia which it creates, i.e., on central and peripheral inhibition of the nervous system.

PROTECTION OF THE ORGANISM AGAINST AGGRESSION

Potentiated anesthesia is above all a method of prophylaxis against shock, traumatic illness, or surgical shock. Among the dysfunctions that appear in an organism under stress, it is necessary to distinguish those which depend directly on the stressor agent (tissue or organic attrition) and constitute the "lesion syndrome" from those disorders which are the result of the organism's reaction to aggression, i.e., the reaction syndrome. The latter is primarily functional but becomes secondarily organic, as Leriche has taught us to regard it. Secondary lesions of a reactive origin possess an essentially vasomotor mechanism, but a part is also played by the endocrine glands and by diastatic and electrolytic imbalance. In effect, action will be exercised on membrane potential, on collagen, and on tissue permeability, and these effects will be combined with those resulting from the anoxia of vasomotor origin. The resulting lesions may therefore be avoided if the organic reaction to aggression is reduced.

While it often appears that illness is actually the organism's reaction to stress, this does not mean that the original lesion syndrome should not be estimated at

its true value. Thus, it is extremely important in therapy to make the distinction between what belongs to the lesion syndrome and what belongs to the reaction syndrome. Potentiated anesthesia, based on pharmacologic neuroplegia, pretends only to oppose the reaction syndrome and its secondary lesions; it has no pretensions whatever of opposing the lesion syndrome.

The organism's reaction to aggression is often out of all proportion to the causative lesion syndrome and it can result in death from minor organic lesions. Neuroplegia can be of great help in such cases. On the other hand, there are cases where the organism's reaction momentarily preserves the right supply to the cerebral centers and the heart; to suppress the reaction would lead to collapse and death.

For example, in cases of severe hemorrhage, the organic reaction is essentially that of peripheral vasoconstriction temporarily permitting sufficient vascularization of the centers, lungs, and coronaries at the cost of a renal and hepatic anoxia, which can secondarily result in death. The suppression of this reaction by neuroplegia without re-establishing the blood volume brings the risk of collapse and death. Contrarily, if the blood volume is re-established at the same time as the vasomotor reaction is suppressed, the physiologic equilibrium is re-established and anoxia prevented in the peripheral organs, particularly in the liver and the kidneys. Therefore, neuroplegia is of use only if the therapist maintains or re-establishes the physiologic equilibrium, i.e., if he counteracts the lesion syndrome that originally engendered the organism's reaction to aggression.

When the lesion syndrome is predominant, whether primary or secondary to the reaction syndrome, only a more or less profound metabolic decrease, or decelerated life as produced by artificial hibernation, can hold out the hope of gaining enough time to save a situation which otherwise appeared hopeless.

Having considered hemorrhage as an example, the occurrence of infection can also be discussed. It is obvious that when staphylococci are placed in a test tube, even in an appropriate culture, they will not produce a furuncle. For that to appear an organism is required which is able to react to the staphylococci. If, then, in that organism the means of reacting against the microbe are suppressed, in effect what we call the disease will also be suppressed. Halpern and Reber demonstrated this experimentally with derivatives of phenothiazine. Having infected rabbits with the typhus bacillus, these researchers used phenergan to suppress local and general reactions to the microbe; their animals later died of septicemia in larger numbers than the controls. In that case, the lesion syndrome finally prevailed as the reaction syndrome was absent.

In cases of infection, therefore, neuroplegia can only be effective if the microbes are attacked simultaneously with, for example, antibiotics. On the other hand, neuroplegia is capable of affording protection against the syndrome of infectious diseases which produces a disordered reaction to the microbial attack. Numerous clinical observations have in fact illustrated the views we have advanced.

BIBLIOGRAPHY

1. Laborit, H.: L'Anesthesie facilitée par les Synergies Médicamenteuses, vol. 1, Masson & Cie, 1951.
2. Taverna and Sagrepanti: Minerva med. *59*:260, 1953.
3. Terzian: Rassegna di neurol. veget. 4-5:211, 1952.
4. Laborit, Huguenard, and Alluaume: Presse méd. *10*:206, 1952.
5. Jentzer: C. R. Soc. de biol. 11-12:876 (June) 1952.
6. Bobbio: Gior. ital. anest. e analg. *18*:560 (Sept.-Oct.) 1952.
7. Castaigne: Soc. med. chir. et phar. de Toulouse (July 1) 1952.
8. Aron et al: Bull. Acad. nat. méd. *137*:417–420, 1953.
9. Li Voti: Minerva med. *94*:1573 (Nov. 24) 1953.
10. Cahn et al: An. et Anal. *1*:80 (Jan. 27) 1953.
11. Marquardt: Therapie. *6*:787, 1953.
12. Laborit, H., and Leger, L.: Presse méd. *27*:142 (April 29) 1950.
13. Laborit, H.: Anest. et anal. 3:454 (Mar. 8) 1951.
14. Laborit, H.: Presse méd. *47*:851 (July 22) 1950.

LIST OF GENERIC AND TRADE NAMES OF
LYTIC DRUGS USED FOR ARTIFICIAL HIBERNATION

4560 RP—Laboratory code number of a derivative of dibenzoparathiazine. 10-(3-dimethylaminopropyl)-2 chlorphenothiazine HCl. Generic name: chlorpromazine HCl. Trademarks: largactil, ampliactil, amplictil, hibernal, megaphen, thorazine.

Casantin—See diparcol.

Chlorpromazine—See 4560 RP

Demerol—See dolosal.

Diparcol—Proprietary name of 10-(2-diethylaminoethyl)phenothiazine HCl. Possesses both parasympatholytic and sympatholytic action. Generic name: diethazine HCl. Other trademark: casantin.

Dolosal—N-methyl-4-phenyl-4-carbethoxypiperidine HCl. Other tradenames: demerol, dolantin, pethidine, dispadol, dolvanol.

Fargan—See phenergan.

Largactil—See 4560 RP.

Mephedine—Proprietary name of meperidine hydrochloride (*N*-Methyl-4-phenyl-4-carbethoxypiperidine hydrochloride). Other proprietary names: demerol, dolantin, dolosal, dolantal, endolat, dispadol, and dolvanol.

Phenergan—Proprietary name for 10-(2-dimethylamino-1-propyl) phenothiazine HCl. Generic name: promethazine. Other trade names: atosil, fargan.

Thorazine—See 4560 RP

Artificial Hibernation

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The reaction of an organism to an outside aggression, e.g., cold, can be inhibited through the neuroplegia caused by what has been termed potentiated anesthesia. In homothermal organisms a uniform temperature is maintained by the peripheral and central mechanisms. The peripheral action consists principally of vasoconstriction which limits the loss of heat by convection; this can be blocked by a lysis-producing drug. The more obscure central mechanism may possibly be activated by a diencephalic, thermoregulating center which increases the production of heat by increasing cellular metabolism. This mechanism is extremely difficult to block.

Weese recently informed us of his experimental work in which he emphasized the essential part played by the lytic mixture—chlorpromazine-phenergan-dolosal*—in preventing a hypermetabolic reaction to cold, an effect which was not produced by numerous drugs used singly. This present study will thus be concerned with neuroplegia, on the one hand, and with hypothermia, on the other—the whole constituting what we have fortuitously called *artificial hibernation.*

The latter aims at producing a hypometabolism capable of efficiently counteracting lesion-causing syndromes which would be rapidly fatal in all other circumstances. Neuroplegia alone is insufficient to achieve this; in some cases, where there is a serious, uncorrected lesion-producing syndrome, it can oppose the reaction syndrome and precipitate death. However, by reducing the metabolic requirement of tissues, one can hope to give the organism enough time to re-establish homeostatic equilibrium, correct internal disorders, and to allow treatment of any organic or tissue lesions. Quite naturally, if the original lesion-producing syndrome is irreversible and affects elements essential to the life of the total organism, any survival time gained will be futile, and the eventual return of vital processes to their normal intensity will result in organic dissolution and death. It follows that artificial hibernation can have only a limited application in either prophylactic or curative therapy and can only be concerned with serious aggressions accompanied by a dominant lesion syndrome.

Jaulmes, Bénitte, and Laborit demonstrated in the case of hemorrhagic shock that an animal maintained by hemorrhage at the low arterial pressure of 40 mm.Hg. dies rapidly under a drug-induced neuroplegia if the blood mass is not restituted. On the contrary, if the neuroplegia is combined with a hypothermia which lowers the animal's metabolism from 40 to 60 per cent, it will not only survive but will also tolerate the aggression much longer without later succumbing to the secondary effects of prolonged vasoconstriction in the kidneys, liver, and peripheral capillary system. The vasoconstriction will have been effectively suppressed by the neuro-

* See list of drugs on page 320.

plegia, while the lowered tissue demands will have been met by the reduced blood volume.

The problem can also be viewed from the standpoint of a diminished exchange between the cell and its internal environment, which would explain the results obtained by Jaulmes, Delga, and Richard[2] in using artificial hibernation to preserve dogs that had been submitted to cyanhydric intoxication. The same problem, although more complex, was seen in the experimental traumatic shock induced by Jaulmes and myself with co-workers, following the technic of Hermann and Jourden.[3, 4] There also the protective effect of hypothermia in association with neurovegetative stabilization was established.

NEUROPLEGIA

While largactil* has a great usefulness, it should not be forgotten that a number of artificial hibernations have been induced experimentally and clinically without it.[5, 6, 7] Courvoisier and co-workers first studied this substance for its possible anesthetic potentiation, having previously established the potentiating action of certain derivatives of phenothiazine, such as phenergan and diparcol. Later, I established its wider indications in general pathology. It must be emphasized, however, that this substance by itself does not induce any significant hypometabolism if hypothermia is not established while the drug is actively blocking thermoregulation. The blockage is itself incomplete; for that reason, in hibernation, even more so than in potentialized anesthesia, it is indispensable to use lytic mixtures, generally combined with barbiturates (which alone can assure cortical inhibition), if one wishes to obtain a nonaggressive hypothermia. It seems that such a hypothermia can also be realized under suitable conditions with hydergin in place of largactil in the so-called "lytic cocktail," or even by any other multifocal neurologic inhibition.[8]

HYPOTHERMIA

This may be obtained without heavy refrigeration simply by maintaining in a temperature of 64 F. to 68 F. small animals whose surface-volume ratio produces a high thermolysis without compensatory thermogenesis; in the dog this can only be produced by shearing the animal. Similarly, with human beings the use of refrigeration is frequently indispensable if one requires a significant hypothermia. In such cases, the danger is that one may induce hypothermia through thermolysis without adequately blocking thermogenesis; hypometabolism is not produced then. This effect will appear in the thermal graph as a plateau which can be avoided only by injecting more lytic drugs or by a temporary reduction of refrigeration.

CONCLUSION

Neuroplegia induced by potentiated anesthesia, by suppressing certain disordered reactions in the injured organism, is capable of preventing pathologic reactions,

* See list of drugs on page 320.

of which surgery is only one of the etiologic factors. But this requires the operator to keep a close watch on the internal balance, inasmuch as the neuroplegia only moderately reduces the vital cellular processes; their supply of energy must therefore be maintained at a level sufficient to avoid damage. The integral value of the blood mass is one of the factors which must be imperatively maintained.

In the presence of a lesion syndrome, whether directly connected with the initial injury or caused by secondary reactions not reduced by prophylactic neuroplegia, the use of artificial hibernation is indicated. Its ability to decrease the intensity of vital processes may often afford the operator the time required to repair syndromal lesions that might otherwise become irreversible.

BIBLIOGRAPHY

1. Jaulmes, Bénitte, and Laborit: C.R. Acad. Sciences. *234*:372, 1952.
2. Jaulmes, Delga, and Richard: C.R. Soc. Biol. *147*:1220, 1953.
3. Jaulmes: Journées Transfusionelles de Genève, Sept. 13, 1953.
4. Bénitte, A. C.: Archiv. f. exper. Path. u. Pharma. 222:1954.
5. Laborit and Huguenard: J. de Chir. *67*:631 (Aug.-Sept.) 1951.
6. Cahn et al: Soc. Fçse. d'Anesth. et d'Analg. Nov. 24, 1953.
7. Campan: Congrès des neuro-chirurgiens de langue française. Algiers, 1954. In press.
8. Li Voti, P.: Minerva méd. *94*:1573 (Nov. 24) 1953.

General Technic of Artificial Hibernation

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Neuroendocrine inhibition, which can be effected in all degrees of intensity, is based on the general therapeutic principle of diminishing, rather than of increasing, the amplitude of organic reactions. On that basis, the simple administration of a synthetic antihistamine such as phenergan* in anesthetic premedication is already one method of using "hibernotherapy," which I proposed some years ago and which has now become standard procedure. A more complete blockage with chlorpromazine makes possible potentiated anesthesia, but a much stronger neuroendocrine inhibition is produced only by active refrigeration and artificial hibernation. Its standard and simplified technic is the one described here.

Administer by the oral route, on the evening before the intervention, 0.05 Gm. phenergan and 0.10 or 0.20 Gm. phenobarbital. This affords the patient a calm night and avoids discharges of epinephrine resulting from fear. Three hours before the intervention, inject intramuscularly 0.05 Gm. phenergan and 0.10 Gm. dolosal. A polythene catheter is then placed intravenously and a one and a half hour drip introduction of saline serum containing 0.05 Gm. chlorpromazine and 0.05 Gm. phenergan is made. At the same time, a syringe is used to take up 0.10 Gm. dolosal, of which 0.5 cc., i.e., 0.025 Gm., is injected in the perfusion tube.

Of the three drugs used, we consider dolosal to be the only dangerous one; in certain doses and in some subjects, it unpredictably provokes a noxious respiratory depression. The patient's reaction to the first injection of dolosal will determine whether or not to continue administration of 0.10 Gm., the full dosage.

It should be pointed out that unconsciousness, which is an excellent sign of the patient's readiness, is not necessarily a parallel reaction of the neuroendocrine inhibition. An unconscious state is desirable because it generally permits intubation without anesthesia or with a minimum of general anesthesia, followed by a minimum anesthesia facilitated by a good curarization. But what is mostly desired is a good vegetative stabilization, and that depends on vegetativolytic drugs such as chlorpromazine and phenergan.

A light and progressive drop in arterial pressure is produced, and it must not go lower than 90 or 100 mm. Hg. The pulse is slowed down and becomes stabilized around 80, and there is also a diminished respiratory rate that must remain ample. The color of the ungual bed and the capillary pulse are excellent; the skin coloration remains pink.

As soon as consciousness is lost, refrigeration can begin. In current practice, it is sufficient to use six or eight ice bags if a rectal temperature of not lower than 93.2 F. is required. The bags are applied at the vascular crossways and the intended

* See list of drugs on page 320.

surgical region. If the vegetative blockage is incomplete, there will be a slight rise in tension with acceleration of the pulse; these often precede some quivering of the masseter and pectoral muscles. In such cases, a deeper blockage should be effected either by accelerating the perfusion of the lytic drugs, by intravenously injecting a few centigrams of pentothal, or by administering some inhalations of a strong anesthetic. The ice bags can also be removed momentarily, either partially or totally.

The patient is ready for the intervention when the pulse, tension, and respiration remain below their initial levels for about 30 minutes. At that point the rectal temperature is usually about 95.9 F.—this will continue to descend during the intervention. Intubation is performed under a local anesthetic and curarization; it may sometimes require complementary anesthesia, intravenously or by inhalation. Usually this is the only anesthetization required—particularly in old people, the remainder of the intervention being done under pure oxygen.

Two important points should be noted. If the intervention is highly hemorrhagic, continued perfusion should be done with 0.025 Gm. chlorpromazine per liter of replaced blood. Otherwise there are the risks of seeing the vasomotor protection disappear and of producing a peripheral vasoconstriction as a reaction to the surgical shock. As this vasoconstriction diminishes the capacity of the circulatory system, it will prevent the replacement, volume by volume, of the blood loss and provoke the risk of a ventricular surcharge and acute edema of the lungs. Maintenance of the vegetative inhibition can prevent this accident, as was demonstrated by David in using the method in exsanguinotransfusion.

The accident in question is particularly to be feared in the case of rapid and massive intravenous transfusions which tend to oppose violent arterial hemorrhages. Peripheral vasoconstriction having been interdicted, vascular resistance remains normal and the maintenance of arterial pressure at its initial value shows that the blood volume is being maintained. Hypertension, especially with a stable pulse, then indicates that the transfusion is too heavy. However, a lowered tension, even with a nonaccelerated pulse, indicates that there is insufficient replacement. Outside of these eventualities, arterial pressure will hardly be influenced by anything other than a change of posture which provokes declive drainage. Venous pressure is a useful check on the repletion of the returning circulation and on the dextral heart.

If the intervention lasts more than an hour, it is preferable, apart from any hemorrhage, to continue the neuroendocrine inhibition by small doses of chlorpromazine injected in the perfusion tube or diluted in the saline solution. In such conditions, one is struck by the constancy of the pulse, tension, and respiratory rates, despite extremely serious surgical stress on very deficient organisms. Finally, the patient should be returned to the ward with his head lowered, and maintained in that position for 24 hours.

POSTOPERATIVE PROCEDURE

Venous perfusion must be maintained. The quantity and quality of the perfused liquid will be established on the basis of the hydroelectrolytic balance of the blood.

The quantity will be lowest in patients who sleep calmly and neither transpire nor vomit. Two liters of serum, of which 1.5 liters is glucosed and 0.5 is saline, are the average quantities which are rarely exceeded. Our practice is to divide the doses of drugs to be administered in 24 hours by continuous drip.

For the first 24 hours, the average doses are: chlorpromazine, 0.25 to 0.40 Gm.; phenergan, 0.10 to 0.15 Gm.; dolosal, 0.10 to 0.20 Gm. The patient is covered only by a sheet. A few ice bags are kept on the operative region. Graphs for pulse, tension, respiration, and temperature are established every hour or every two hours. These must remain stable at levels lower than normal. The course of the graphs will dictate the rhythm of perfusion, which will have to be accelerated or decelerated.

Two days after the intervention the same dosages can be administered. Owing to tolerance, their efficacy will be lowered and the patient will progressively return to consciousness. Amnesic and analgesic, he will most frequently ask when he is to be operated upon. At that point, it is preferable to administer heparin intravenously in dosages of 300 to 400 mg. for 24 hours, while maintaining a check on the blood crasis. In effect, the hypocoagulatory effect of the drugs is followed at the moment of their withdrawal by a stage of hypercoagulability which favors thrombosis. The risk of secondary hemorrhage as the result of heparin is actually much lower after the forty-eighth hour.

The dehibernation of the patient frequently causes his re-equilibration to show a hyperthermal graph with an accelerated pulse, usually not troublesome. When the patient is agitated, we administer 3 to 6 mg. of thyroxin in 24 hours, for we have been able to correlate some of these accidents with a hypothyroid crisis. Hydergin in doses of three ampules intravenously in 24 hours by perfusion is also useful.

ADDITIONAL CARE

The inhibition of salivary secretion causes dryness of the mouth which can be relieved by frequent moistening with a damp cloth. Urine retention is customary and requires drainage twice daily. Diuresis is excellent. Intestinal movement is resumed as soon as the drugs are discontinued. The abdomen remains flat without meteorism or pain. If palpation is painful and provokes a reaction in the hibernated patient, it is a sign of some complication.

Pulmonary complications are an exception. It should be kept in mind that some bronchorrhea may be met in patients sensitive to phenergan; this will disappear when the drug is discontinued. We habitually administer aerosolized privine* (or nor-epinephrine) to cause local blockage of the bronchial circulatory system.

SUPPORTIVE THERAPY

For some time I have used pituitary somatotropic hormone (growth hormone) preoperatively and postoperatively in order to increase protein anabolism and to counteract postsurgical nitrogen catabolism. Injection of 100 Evans units intra-

* Privine hydrochloride, a proprietary vasoconstrictor and nasal decongestant.

muscularly of the hormone is made on the evening before intervention, and 100 units are injected intramuscularly during the following two days. In debilitated and chachectic patients the same treatment is used in three day periods every four or five days. The reduction of nitrogen catabolism is observed in the parallel decrease of blood and urine urea. The pathologic action of the hormone produces various thermal conditions which are easily controlled by synthetic antihistamines. Androgens have also been used, although their protein anabolic effect is much less apparent.

Prostignin in daily doses of two ampules intramuscularly favors the anabolic effect of the parasympathetic system. Treatment with vitamins (vitamin C and the vitamin B complex) is also recommended.

Believing as I do in the beneficial effect of postoperative sleep, and knowing that some patients are impervious to dolosal, there is no hesitation in administering pentothal intramuscularly in doses of 0.50 Gm., with a total dose of 1 to 2 Gm. in 24 hours. These doses, potentiated by chlorpromazine, are sufficient to maintain sleep and the desired calm.

Antibiotics can be administered according to the usual procedure. Hibernation reduces organic reaction to microbial agents and thereby reduces what are customarily called the signs of infection (pus is decreased, inflammation disappears, and general signs are improved). At the same time, hibernation exercises a relatively minor effect on the germs, and it is therefore of value to oppose their development with the use of antibiotics which have been tested for their potency against certain organisms.

Application of Artificial Hibernation to War Surgery in Indochina

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Early in 1952, Dr. Henri Laborit proposed the use of lytic and pharmacodynamic methods, particularly the method of "artificial hibernation," for the prevention and treatment of traumatic shock, a major problem in war surgery. In October of that year, Dr. Nicol, Chief Naval Surgeon at Haiphong, and I, working in Hanoi (North Vietnam), obtained satisfactory results which warranted a closer study. Late in March, 1953, Doctors Laborit and Huguenard came to Vietnam on a mission and established the basis of a standard method that has since become common practice both in Saigon and Hanoi. The present study is based on observation of approximately 300 cases.

GENERAL REMARKS

In modern warfare, the violence of the explosives and the innumerable offensive and defensive devices produce a large number of multiple injuries including blast lesions. In many cases, shock is accompanied by neurovegetative disorders, such as sudden loss of blood or the slow continuous loss of blood which is even more serious. To these must be added the strain of combat, fatigue during evacuation, the climate, and other stresses of a tropical country. Each of these factors influences the therapeutic method required, starting at the battlefield first-aid station and continuing to the Mobile Army Surgery Hospital (MASH).

It must be pointed out that war surgery is mass surgery and that evacuation from the battlefield to the first hospital will often be made in several steps.

At all stages between the evacuation from the battlefield to the hospital, the wounded often number beyond the capacities of the medical personnel and the available supplies. For that reason, it is desirable to standardize treatment for shock in such a manner that it can be applied by as many persons as possible, anywhere, and in any circumstances. Although artificial hibernation is obviously not a method that can be applied in all circumstances, it has opened a new field of therapy of great help in certain clinical cases.

TECHNICAL CONSIDERATIONS

When properly used, artificial hibernation can be a precious aid in preventing surgical shock. It provides the patient with relaxation and comfort that could not be obtained otherwise. But it also undeniably imposes certain obligations on the operator.

Whether artificial hibernation is used to prevent shock or to treat shock (either in transportation or in surgery), it requires particularly experienced and skilful

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* Consulting Surgeon of France's Armed Forces in the Far East. Dr. Chippaux was recently working in the underground hospital of the French fortress of Dienbienphu.

reanimators. Reanimation of a shocked patient by classical methods is difficult enough—the new method requires experienced physicians and a trained personnel. The reanimation technic derived from Dr. Laborit's work provided some surprising clinical evidence. As Professor Gosset stated: "It is an improvement which brings something genuinely new in the treatment of shock." Some of the results obtained in war surgery have been revolutionary.

The wounded man is anxious, delirious, and agitated; yet, a few moments later the same man can be put under a prolonged hypnosis, to which is added hypothermia, and the neurovegetative processes are restored to a harmonious function. However, there is a danger here, for the patient may, in the words of a stretcher-bearer, look "half dead." This may lead to an incorrect diagnosis, since the surgeon who puts the patient into hibernation is not the one who will treat him at the hospital.

As soon as hibernation has been induced, the patient must be under constant care if he appears unstable. Instability can be chronic in an overwarm atmosphere without air conditioning, such as the climate of Vietnam in the summer. In the tropical zone, artificial hibernation must be done in an air conditioned locale. In the winter, the transportation of a hibernated patient from the front to the medical center is feasible, but in the summer the problem is greater, unless the evacuating helicopters, ambulance planes, and cars are also air conditioned to maintain the patient's homeostatic equilibrium.

Artificial hibernation requires more personnel than an ordinary reanimation center because surveillance is closer and lasts longer—from 36 to 48 hours. The reanimators must have wide clinical experience and long practice not only in the stabilized stage of hibernation but particularly in the warming-up period. We consider the latter to be the critical time, because in cases of multiple injuries from blast, neurovegetative reconnection is not as easy as in nonshocked, or only slightly shocked, patients who have been hibernated in preparation for lengthy surgery. The warming-up period is in fact a time when accidents and sudden complications can occur.

We conclude from this that the standard artificial hibernation method established by Laborit and Huguenard cannot be used as a general treatment adaptable to all cases in a tropical zone because of various difficulties, such as transportation problems and the technical and material demands of the method.

NEUROVEGETATIVE DECONNECTION

Aside from artificial hibernation, we have some observations to make on the lytic methods indicated by Laborit and for which the term "neurovegetative deconnection" has been adopted. This consists of producing with a mixture of neuroplegic drugs a rather profound twilight sleep with a greater or lesser blockage of the neurovegetative system.

We commonly use phenergan-dolosal* for a moderate vasoplegic and neuroplegic action, alone and in combination with other lytic drugs such as novocaine, sparteine, and diparcol. The two products first mentioned are far less vasoplegic than some

* See list of drugs on page 320.

other lytic drugs, such as chlorpromazine (4560 R.P., largactil), and the methonium salts. Intramuscular and hypodermic injections of these drugs are preferred to the intravenous route.

In most cases, in addition to producing greater steadiness than morphine, this type of prenarcosis deconnection has the faculty of potentiating all the anesthetics that can be given at the first-aid station or at the clearance base; it also facilitates postoperative care which, in the case of wounds, is often complex and lengthy. In our own experience based upon several thousand cases, we have met with neither positive contraindication nor accidents.

TACTICAL FACTORS IN WAR SURGERY

It is clear from the foregoing that standard artificial hibernation cannot be practiced unless the mobile army hospitals are equipped with qualified medical personnel and air conditioned rooms. Systematic artificial hibernation is therefore obviously impossible at advanced first-aid stations.

The individual lytic syrette (phenergan-dolosal-largactil), at one time advocated by Dr. Laborit, appears to be useless on the battlefield for the conscious wounded soldier who is awaiting assistance and who must be able, perhaps without help, to find shelter. Also the seriously wounded man, threatened with shock, is not able to use a disposable syringe on himself.

There is no doubt, however, that a neuroplegic injection would help to cope with any shock that might be aggravated by transportation.* On the other hand, the neuroplegia produced by lytic drugs is accompanied by a marked vasoplegia capable of aggravating, during transportation, the disequilibrium of the circulating blood whether or not shock is present. Such vasoplegia can only be counterbalanced by transfusion, which is difficult or practically impossible to effect on the battlefield. If there is too great a delay between the vasoplegia and the transfusion, the former can lead to a fatal drop in blood pressure.

From our experience in North Vietnam during the winter of 1952–53 and the summer of 1953, we can emphasize the advantages of producing an early neurovegetative deconnection with lytic drugs. The sooner the injection is given, the better the wounded can stand transportation to the first-aid station and later to the mobile hospital. The best results would be obtained if the injection could be given on the battlefield or when the wounded are in the helicopter enroute to a hospital.

Can artificial hibernation be applied at this stage? An experiment was made at Nassan and Laichau during the winter of 1952–53 in an underground mobile hospital. About 30 near-shock cases, mostly with multiple abdominal injuries, were put under hibernation and operated upon immediately. A number of others were evacuated and operated upon at the central hospital at Hanoi, after a flight of one to one and a half hours by a DC3.

The fine results obtained at the start were attributable to the fact that the mobile hospital was located near an airfield where a DC3 could land and take off,

* Means for evacuation are still inadequate in Indochina, as helicopters are often prevented from landing by the nature of the terrain: rice fields, jungles, and mountains.

and to the second fact that there were qualified nurses aboard the planes. The experiment was also carried out in the winter in an outside temperature below 68 F. In the summer, however, the temperature rises to 104 F. and higher, making artificial hibernation impossible because of the inability to maintain hypothermia. Also, in the summer, the mobile hospitals were under canvas and liaison was done by road or small aircraft with no nurses aboard. It was found that even a fast trip of less than an hour from a cool region, where the wounded were put under hibernation, to a warmer zone (such as the Red River delta) provoked a typical stress syndrome resulting in death from hyperthermia.

ARTIFICIAL HIBERNATION IN TRAUMATIC SHOCK

It is difficult at the present time to determine the exact value of artificial hibernation in comparison with the classical methods of reanimation in the treatment of traumatic shock.

The value of transfusion in the treatment of shock in war surgery hardly needs emphasizing. Whatever the cause of the circulatory disequilibrium, it is important to restore the blood volume as soon as possible; in the majority of cases, the efficient standardized technics of today are the method of choice. But this method fails in some cases, especially in the presence of peripheral vasoconstriction or intense and prolonged neurovegetative instability caused by the initial stress or by repeated aggression during transportation. Classical reanimation methods also fail when prolonged surgery follows the initial state of shock.

In such cases, the only hope lies in artificial hibernation. With it, we have in our experience been able to bring patients out of shock and enabled them to support the required surgery. But it should be noted that the sudden vasoplegia caused by the lytic drugs in the standard Laborit method must be closely watched. Artificial hibernation should only be undertaken when an abundant and continuous transfusion accompanies the progress of vasoplegia.

In practice, we wait for about one hour before deciding on hibernation. In most cases, transfusion alone increases and stabilizes blood pressure sufficiently to permit surgery without major risk. After an hour, if blood pressure is neither increased nor stabilized, or when the patient has been reanimated with difficulty and has to undergo lengthy major surgery, hibernation is indicated.

Even when a large transfusion has been given and the blood pressure either does not increase or increases only slightly, the real gravity of the neurovegetative disorder is shown and the problem becomes alarming. Are we then authorized to introduce a powerful vasoplegic mixture, which is also a neuroplegic one?

Up to the last few months, we introduced the mixture only when blood pressure was at the arbitrarily established point of 6. Since then, in a few desperate cases, where the blood pressure remained at zero despite three or four hours of transfusion, we tried using the lytic mixture. To our surprise, the blood pressure became measurable and authorized surgery—and in all these cases we had previously transfused several liters of liquid.

It would appear, therefore, that the lytic mixture caused a better distribution of

the blood volume which had become blocked in the splanchnic regions and had almost disappeared from the peripheral vascular branches owing to intense vasoconstriction. This improved blood distribution would also explain why artificial hibernation does not require more blood than ordinary reanimation, as was noted both in Saigon and Hanoi.

While artificial hibernation helps to solve the fluid problem in shock, we should also underline its value in cases of threatened hyperthermia and intractable agitation, where the gravity of the neurovegetative disorder is clearly shown. In such cases, classical reanimation methods only too often fail; in tropical climates that type of disorder may bring death in a few moments.

With artificial hibernation we were able to obtain a permanent thermal decrease and often produced improvement long enough to give hope of recovery. However, we must admit that in most cases of multiple fractures with splanchnic lesions and infection by rice-field mud in the muscles, we have helplessly watched the failure of our efforts. Irremediably affected in their vital parenchyma by irreversible lesions, patients died from one or more associated complications of a confused clinical nature.

It would be deceiving at present to present any statistics of deaths in our use of artificial hibernation in war surgery. Those who died were in most cases beyond all therapeutic aid. In regard to recoveries, nothing can prove that classical reanimation would not have by itself been sufficient in the majority of cases. We can say, however, that in about 10 per cent of desperate cases where transfusion failed, artificial hibernation allowed us to act. If systemic recovery was out of the question, at least there was some hope for a few days.

This fact alone permits us to state that artificial hibernation can now be included in the therapeutic arsenal of reanimation. But it still requires research, inasmuch as there are several varieties of hibernation and neurovegetative deconnection presenting a wide field for experiment with pharmacodynamic drugs. Although not constantly successful, artificial hibernation has produced unexpected recovery in borderline cases.

Tissue Respiration During Artificial Hibernation

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The variations induced by low temperatures on the functional activity of the tissues depend on the intensity and duration of the low temperature and also on the type of tissue being refrigerated. Tissues with a high proliferative capacity offer a greater resistance to low temperatures than tissues with lesser proliferative capacity, particularly if they belong to homeothermal organisms which are so sensitive to refrigeration that they very easily undergo irreversible alterations. Different cells and tissues respond differently when subjected to low temperatures: every type of cell and tissue possesses a certain minimum temperature, the so-called "biologic zero," which, when reached, arrests the specific cellular functions, e.g., the ameboid movements of white cells or the conduction capacity of stimuli along nerve fibers.

In artificial hibernation (according to the method of Laborit and Huguenard) we put the organism under refrigeration and at the same time block the neurovegetative system with appropriate drugs, of which the most active seems to be chlorpromazine. Such a block, besides hindering the organism's defence mechanism, is capable by itself of decreasing oxygen consumption in the tissues owing to the fact that the block inhibits impulses in the adrenergic fibers, with consequent inhibition of the production of epinephrine, which is a strong catabolic factor.

With the object of controlling the forestated concepts, we have studied, following the manometric technic of Warburg, the comportment of tissue respiration during artificial hibernation.

Here are some of the results obtained in previous experiments regarding the action of chlorpromazine on the oxygen consumption of different tissues. This drug decreases the consumption of oxygen, e.g., in the kidney and in the liver, because while acting on the thermoregulatory center it decreases body temperature and thus lowers oxygen consumption of the tissues mentioned. But for nervous tissue the mechanism is different, i.e., chlorpromazine decreases oxygen consumption independently of the degree of temperature. The decrease *in vivo* and *in vitro* is obtained through the direct pharmacologic action of the drug on the cells, and it is the same as that obtained by refrigerating to 86 F. This action has been demonstrated to be reversible.

These observations seem to be of great interest in the protection of nervous tissue which is very sensitive to anoxia; it is precisely that protection that we seek in cardiac surgery through the use of artificial hibernation.

It is our opinion that the various methods of hypothermia proposed are not yet the best methods to obtain a temporary arrest of the blood flow and of oxygenation in the nervous centers. The best of the various methods proposed is the Laborit method (neurovegetative block plus refrigeration) even if this is not absolutely without

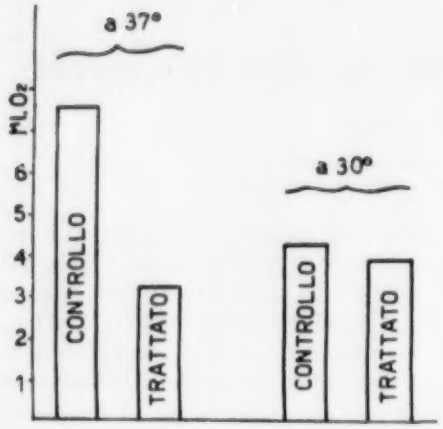
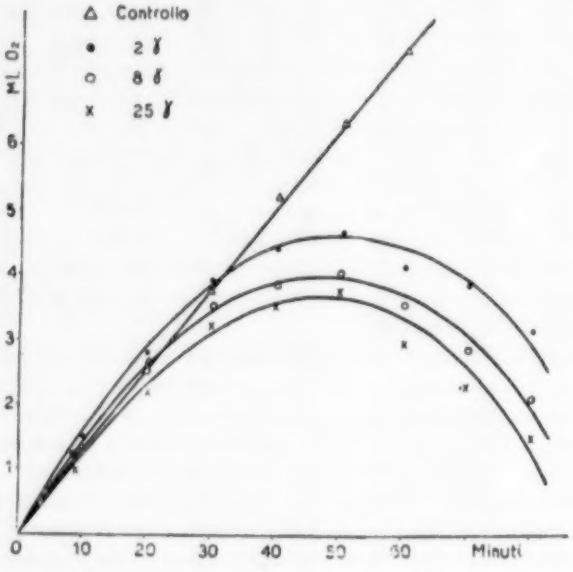


FIG. 1. (left) Consumption of oxygen during the first hour of the experiment (at 37 C. [98.6 F.] and 30 C. [86 F.] respectively) in the cerebral cortex of a white mouse treated *in vivo* with largactil. The oxygen consumption is expressed in microliters and is estimated per 1 mg. of dry substance.

FIG. 2. (below) Consumption of oxygen in cerebral cortex of a white mouse treated *in vitro* with 2γ, 8γ, 25γ of largactil in relation to the time (reading every 10 minutes). Consumption is expressed in microliters and is estimated per 1 mg. of dry substance.



danger, as was observed in many animals who survived cardiac surgery but died later from injuries caused by the low temperatures. Recently, Laborit proposed to include somatropic hormone with the agents used to induce artificial hibernation. We have not yet experimented with this new method, but we believe that the search for drugs which might decrease tissue respiration, especially in nerve tissue, with the same results as those obtained with low temperatures, is worthy of the most serious attention.

BIBLIOGRAPHY

1. BERTI, T., AND BALESTRIERI, A.: Boll. Soc. ital. biol. sper. 29:632, 1953.
2. DI MACCO, G.: Patologia Generale, Ed. Minerva Medica, Turin, 1951.
3. LABORIT, H.: Favre, R., et al.: Presse méd. 61:1249, 1953.
4. LABORIT, H., AND HUGUENARD, P.: J. de chir. 67:631, 1951.
5. PERUSSO, L., AND FORNI, R. B.: Presse méd. 61:1463, 1953.
6. TOSATTI, E.: Med. internaz. 61:1,1953.

Renal Function During Artificial Hibernation

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Artificial hibernation is being increasingly used in the surgical, medical, pediatric, and neuropsychiatric fields and many studies have been made of metabolic changes, cellular respiration, the endocrine system, the cardiocirculatory functions of the body under artificial hibernation. Studies of one of the most important homeostatic mechanisms, the renal function, have been rather uncertain and confusing. Our present report on renal function under artificial hibernation made use of the most recent methods of investigation which allow selective determination of the glomerular and tubular functions and of the quantity of blood flowing through the kidney.

In our experiments we used male dogs ranging in weight from 14 to 18 Kg., placed under fasting basal conditions on the evening preceding the experiments. The dogs were previously trained to maintain a supine position and to support vesical catheterism, so that any variation depending on the emotive state, ureteral spasm, vesical reflexes, and postural reflexes could be eliminated during the experiments. These dogs were hibernated at a 77 F. body temperature, following the method of Laborit (mephedine-phargan-largactil* refrigeration). Under basal conditions, and during the entire period of artificial hibernation, the values of glomerular filtration and tubular reabsorption were determined with the creatinine clearance test, and the renal plasmatic flow with the para-aminohippuric acid test.

The results of our study demonstrated that during artificial hibernation, renal function is altered by a decrease of glomerular filtration and an increase of tubular reabsorption, while the plasma and blood flow and the plasma/blood cells ratios are decreased.

First to be noted is the great influence exerted by the body temperature on the creatinine clearance values, which are decreased at a high level of hibernation. Other experiments, however, showed that refrigeration by itself should increase these values through the hypertonicity of the afferent glomerular arteriole. Therefore, other factors and mechanisms must be responsible for such a reduction in the creatinine clearance, i.e., the decreased arterial pressure and the reduced renal blood flow. These two factors together are sufficient to provoke a fall in the values of glomerular filtration to levels low enough to modify the normal diuretic rate of the kidney. On the other hand, the increased tubular reabsorption is to be related to the neuroendocrine variations induced by the artificial hibernation (adrenergic fibers block, decreased hypophysal, suprarenal and thyroid functions) and at the same time related to the reduced volume of filtration and reduced flow in the tubules.

* See list of drugs on page 320.

The lowered plasmatic and blood flow is directly related to the decreased blood volume which sets in during artificial hibernation.

Our investigations led us to the conclusion that artificial hibernation, according to the Laborit method, does not produce any organic alteration in the kidneys and that the functional modifications observed should be related to the modified neuro-vegetative and endocrine conditions (slowing of vital processes) which are caused by artificial hibernation. This is proved by the fact that when the hibernation is discontinued the kidney resumes its normal rate of excretion.

BIBLIOGRAPHY

1. Bobbio, A.; Goffrini, P., and Bezzi, E.: Presse méd. *60*:1708, 1952.
2. Ciocatto, E.; Bianchetti, E. et al.: Boll. Soc. Piem. Chir., 22:665, 1952.
3. Laborit, H., and Huguenard, P.: J. de chir. *67*:631, 1951.
4. Martignoni, F., and Dovanti, S.: Arch. Sci. Med. *92*:5, 1951.
5. Smith, H.: The Kidney. Oxford Univ. Press, 1952.
6. Tosatti, E.: Rass Clin. Scientifica. *28*:363, 1952.
7. Tosatti, E.: Med. internaz. *61*:1, 1953.

Pharmacologic Hibernation in Lung Surgery

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The former dangers of the open thorax, which occurred mainly in respiratory disturbances with resulting hypoxemia and hypercapnia, have been largely eliminated through endotracheal anesthesia with controlled respiration. The safe elimination of intrapulmonary pressure and the relative immobilization of the mediastinum have helped to avoid sudden pressure changes and hemodynamic hindrances to pulmonary perfusion. When anesthesia with ether was deep enough, the supply of oxygen to the body sufficient, and the elimination of CO_2 adequate, cases of reflex cardiovascular disturbances were extremely rare among our patients. So-called vagal reflex mechanisms, which may be seen when reflexes insufficiently controlled at the time of intubation,[1] during endobronchial aspiration,[2, 3] or in the form of hilus reflexes during the supply of the pulmonary root, are not to be feared if the blood pressure and saturation are normal. Ordinarily harmless vagal reflexes have a completely different effect when one considers hypoxemic, hypercapnic, asphyctic, or ischemic complications. Numerous authors have proved in electrophysiologic studies that anoxemia and hypercapnia stimulate vagal reflex activity.[4–13]

Despite good ventilation, a primary anesthesia and operational mortality continued to hamper lung surgery. The causes were usually sudden blood losses, which could not be replaced with the necessary speed, or disturbances of the gas-exchange mechanism, that were not safely avoided despite aspiration facilities and special endobronchial anesthesia. Hypoxemia was also brought on by complications caused by excessive reduction of the respiratory reserves. The final result of circulatory or respiratory hypoxia consisted of cerebral coma and a complete collapse of circulatory regulation. Although unconsciousness and collapse were sometimes reversible, an unfortunate end could not always be avoided.

Recognizing the importance of an optimal oxygen supply, we soon accepted the theories of Laborit and Huguenard. By the use of such lytic drug combinations as atosil,* megaphen, and dolantin in the area of the end organs, the spinal ganglia, and the central nervous system, we attempted to dull or eliminate circulatory reflexes, which occur during sympathicotonic collapse with increased peripheral resistance caused by vasoconstriction. The authors also sought to eliminate the adrenergic increases in metabolism that accompany increased oxygen consumption, as well as a reduction of basal metabolism. The lowering of the basal metabolism seemed especially important in lung surgery. The protection against circulatory collapse, obtained through sympathectomy by Freemann et al,[14] Wiggers,[15] and Remington[16] using dibenamin, was also obtained with lytic drug combinations by

*Atosil is a brand of N-(2'- dimethyl-2'-methyl) ethylphenothiazine hydrochloride.

Jaulmes, Bénitte and Laborit,[17] and Fournel.[18] Bénitte[19] emphasized that an amazing resistance against asphyxia as well as an increased period of tolerance in ischemia and illuminating gas poisoning were obtained with pharmacologic blocking of the mediators and through induced hypothermia.

In order to test the ideas of angioparalytic circulatory stabilization, improved safety against damage by anoxemia, and prophylaxis of shock,[20, 21, 22, 23] 5 dogs weighing approximately 35 to 55 lbs. each were anesthetized intravenously with only 20 to 40 mg./Kg. evipen after having received low doses intramuscularly of 1 to 2 mg./Kg. of the lytic drugs, atosil-megaphen-dolantin. A control group of 5 animals was anesthetized by intraperitoneal administration of phanodorn (cyclobarbital) in doses of 60 to 90 mg./Kg. The anesthesia in both groups was maintained in the reflexless tolerance stage. Those dogs which spontaneously breathed pure oxygen from the spirometer were then exposed to sympathicomimetic irritation through the administration of 0.1 mg./Kg. effortil* and 0.015 mg./Kg. nor-epinephrine. After this they were cooled by the application of ice. Figures 1 and 2 show the experimental results of the animal's defenses; the superiority of the new method over ordinary deep anesthesia is plainly evident.†

Pharmacologic blockage provides an unmistakable circulatory stability despite the aggressions of sympathomimetics and cold. This stability is shown in the absence of increased pulse rate, of mean and arterial pressure, of peripheral resistance, which are unavoidable with deep general anesthesia. The angioparalysis produced by megaphen is balanced by an initial increase in the pulse rate and heart output and does not overtax the heart, since the peripheral perfusion resistance is low.

The advantages of lytic drug combinations are also seen in respiratory activity. The normalizing effect of megaphen on the respiration and the use of smaller quantities of anesthetics avoid a depression of the respiratory center and a reduction of the thoracic respiration, which are unavoidable concomitants of deep anesthesia. The comparatively improved respiration in potentiated anesthesia is of great importance in avoiding hypoxemic conditions in lung surgery when the patient must return to spontaneous respiration after the operation. The six to eight hour analgesic effect of lytic mixtures in patients with good respiration is an advantage which cannot be exaggerated, since it eliminates the need to resort to opiates which always leads to a more or less prolonged paralysis of the respiratory center in the postoperative suppression of pain. The difference in respiration can also be observed under increased cooling. During the experiments through the intraperitoneal administration of phanodorn, the dogs were sacrificed between 82.4 F. and 78.3 F., with cessation of respiration. The heart activity continued for 6–10 minutes. In the temperature range under 82.4 F., despite reduced oxygen consumption, the CO_2 accumulations in the exhalation reached 6.5 vol. per cent; this also occurred in nonpathologic acidosis, so that the oxygen-ion concentration fell to 7.0–6.9. Even when the CO_2 accumulation was not fatal, it seemed to contribute to death, as the

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* Effortil is the ethyl homolog of phenylephrine hydrochloride.

† The experiments were carried out under the direction of H. Weese and W. Irmer in the Pharmacological Institute of Bayer, Elberfeld, Germany. We wish to thank Miss E. Gross for her cooperation.

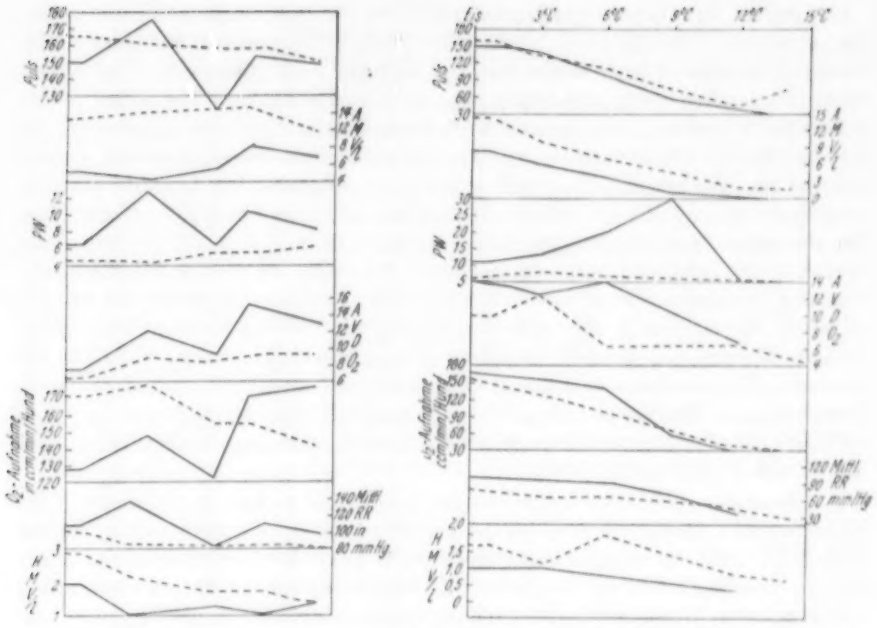

FIG. 1. (left) Mean values in 5 dogs (35 to 55 lbs.) under intraperitoneal phanodorn anesthesia with 60 to 90 mg./Kg. (solid line). Mean values in 5 dogs after administration of lytic combination (1 to 2 mg./Kg. atosil-megaphen-dolantin intramuscularly) in intravenous evipan anesthesia (20 to 40 mg./Kg.) after aggression by sympathicomimetics and ice (dotted line).

Legend: puls—pulse rate.
AMV/1—respiratory volume per minute.
PW—peripheric current resistance.
$AVDO_2$—arteriovenous O_2 difference.
In Vol. % O_2—intake per dog in cc. per minute. Mean blood pressure in mm. Hg.
HMV/1—cardiac output in liters.

FIG. 2. (right) The behavior of equal values under increasing supercooling. Method: electrocardiographic pulse registry. The respiratory volume per minute was calculated in liters, based on respiratory rate and respiratory volume. The respiration occurred from the spirometer in the closed system with CO_2 absorption. The margin of error in respiratory volume per minute and O_2 consumption was 10 to 15 per cent. Peripheral current resistance equals mean blood pressure divided by cardiac output. The percentile oxyhemoglobin saturation was determined electrophotometrically with Brinkmann's hemoreflector (margin of error 1 to 2 per cent) and calculated in accordance with the spectrometically-determined hemoglobin content in Vol. % = arteriovenous O_2 difference and cardiac output according to Fick's principle.

animals submitted to pharmacologic and induced hypothermia did not die of respiratory collapse but, with temperatures ranging from 77 F. to 74.3 F., they died of cardiac arrest with respiratory activity continuing for another 5 to 10 minutes. In view of this improved respiration, the *p*H did not drop below 7.3. The CO_2 concentration in the exhalation was lower on the average by 1.7 vol. per cent.

Oxygen intake was not significantly reduced by the lytic drugs without temperature reduction. The metabolic acceleration produced by sympathomimetics could, however, be avoided more safely than in anesthesia with phanodorn. The advantage of the method can be seen clearly when ice is used as a stress. The higher caloric consumption observed in anesthesia with phanodorn is completely eliminated. In its place there is a temperature-controlled gradual decrease of oxygen intake, demonstrating that the adrenergic increase of oxygen requirements can be safely avoided. A temperature drop of 5.4 F. reduces the oxygen intake from 170 to 120 cc./min./dog. On the other hand, the oxygen intake increases from 128 to 181 cc./min./dog, despite deep anesthesia with phanodorn. According to Grosse-Brockhoff and Schoedel,[24] superficial anesthesia causes the cold aggression to produce an increase of 300 to 400 per cent in the O_2 intake, as long as trembling reactions are present. Cremer, Kramer, and Reichel[25] noted an average metabolic increase of 170 to 340 per cent. The maximum increases of O_2 requirements are 600 per cent, according to these authors. Brocker and Hell[26] found a metabolic decrease in human beings of 14.3 per cent after pharmacologic hibernation, with an average temperature drop of 2.2 F. without application of ice.

The favorable circulatory conditions and the reduced oxygen requirements of the tissues express themselves in a normal arteriovenous O_2 difference, which reaches pathologic levels in animals anesthetized with phanodorn, in view of the heavy oxygen consumption in the tissues and the venous oxyhemoglobin undersaturation. The venous oxyhemoglobin values in both systems are shown in table I.

Aside from the already described differences, it should be mentioned that an unusually strong inhibition of bronchial secretion constitutes an important ad-

TABLE I

Oxyhemoglobin Content of the Venous Blood

	38°	37°	36°	35°	34°	33°	32°	31°	30°	29°	28°	27°	26°	25°	24°	23°
1	43	38	52	32	—	37	—	—	78	—	—	57	—	—	—	—
2	53	11	24	11	12	10	12	23	24	33	37	34	43	—	—	—
3	46	28	35	34	45	46	33	11	23	11	5	—	—	—	—	—
4	—	—	35	35	—	30	—	37	—	41	37	—	—	—	—	—
5	—	42	48	—	16	—	33	—	77	85	69	—	—	—	—	—
	47	30	39	28	24	31	26	24	51	42	37	45	43	—	—	—
6	78	45	74	15	37	63	62	68	43	50	63	45	44	36	36	—
7	—	—	38	24	35	32	51	63	50	56	76	71	61	61	—	—
8	—	55	27	42	23	33	50	50	23	48	45	34	35	28	24	—
9	—	70	71	86	—	65	—	59	—	53	—	—	—	—	—	—
10	71	—	—	54	—	18	11	—	—	23	33	—	—	—	—	—
	74	57	52	44	32	42	43	60	39	46	53	50	45	42	30	—

Numbers 1 through 5—venous oxyhemoglobin values under phanodorn anesthesia.
Numbers 6 through 10—animals under pharmacologic hibernation.

TABLE II

Hypotension Through Pendiomid and after Procaineimide in Potentiated Anesthesia

No.	Wt. in Kg.	Respiration		Pulse		Mean Blood Pressure in mm. Hg.		Hb O_2% Art.		Hb O_2% Ven.		O_2 Intake in cc.		HMV in liters		P	W
		Before	After	B	A	B	A	B	A	B	A	B	A	B	A	B	A
1	19.7	21	21	—	—	100	45	79	93	43	33	144	123	2.0	1.0	50	40
2	22.4	12	14	174	168	140	80	95	94	50	51	185	133	1.6	1.3	87	61
3	18.5	15	25	132	120	120	60	95	95	44	27	92	77	1.1	0.7	100	85
0	—	—	—	—	—	120	62	90	94	46	37	140	111	1.6	1.0	79	62
4	27.0	30	31	162	168	110	70	98	85	63	70	190	201	2.4	6.2	40	11

Animals 1-3—intraperitoneal phanodorn anesthesia (60-70 mg./Kg.). Hypotonia with 1.0 mg./Kg. pendiomid i.v. Animal 4 in potentiated anesthesia (2 mg./Kg. atosil, megaphen and 700 mg. evipan i.v. hypotonia with 10 mg. procaineimide per dog. (Adapted from Irmer-Weese, unpublished.)

vantage in complications during anesthesia and postoperatively. The effective elimination of laryngeal reflexes and bronchospasms should also be mentioned. The lytic drugs also serve as a good prophylaxis against pulmonary edema, a fact that can be explained by the internal angioparalytic bloodletting and the capillary-constricting antihistaminic effect. The application of controlled hypotonia is justified in cases of strong superficial hemorrhages, that dangerously interfere with surgery, or of large blood losses which cannot be replaced quickly enough. In pharmacologic blockages the blood pressure can be better reduced with divided, rapidly successive procaine amide injections of 25 to 50 mg. (maximum of 200 mg.) than with hexamethonium, as can be seen in table II.

Laborit, Huguenard, and van de Walle[27] continually emphasize that hypotension with pure ganglionic blockage agents produces undersaturation of oxygen in the venous blood. Table IV illustrates that this, as well as greater reduction of cardiac output, can be avoided through hypotension produced by procaine, following the administration of lytic drugs.

Our experience with pharmacologic hibernation in intracardial surgery shows the drugs to have a beneficial effect on cardiac reflexes. Arrhythmias directly related to the heart can be eliminated and dangerous ventricular tachycardias decreased. Of special interest was an improved stability of the peripheral circulation and the rare occurrence of sleep caused by cerebral lesions.

Eichholtz, Fleckenstein, and Muschaweck[28] and Zipf[29] demonstrated experimentally that antihistaminic agents reduced the irritability of sensitive receptors in the Bezold-Jarisch reflex. This effect is said to occur even with low doses. According to communications from Dews and Graham,[30] Levitan and Scott,[31] and McCawley,[32] the effect of neo-antergan, pyribenzamine, and benadryl on the vestibule is double that of chinidin. This favorably influences ventricular tachycardia and extra systoles caused by increased sensitivity to irritation. Zipf demonstrated electrophysio-

logically an internal anesthesia of the sensitive cardiac receptors, after intravenous administration of a procaine drug. According to his study, megaphen, which also possesses a strong local anesthetic effect, produces a certain endoanesthesia of the sensitive cardiac receptors and the pulmonary receptors, having also favorable activity on the Bezold-Jarisch reflex. Cahn et al[22] proved that pharmacologic hibernation in animals increased the survival rate after cardiac infarctions originating in coronary obstruction.

Potentiated anesthesia is easily carried out. As to nomenclature, superficially potentiated anesthesia might be called "facilitated anesthesia" and the deep potentiated anesthesia, during which a definite temperature drop occurs, "pharmacologic hibernation." The production of hypothermia by physical cryotherapy and the prolonged continuance of hibernation are only rarely indicated in lung surgery. Pulmonary function and respiratory reserves must be watched, despite the fact that hypothermal oxygen regulation permits even desperate cases to be carried through the acute dangers of the operation and the immediate postoperative complications. If overconfidence leads to risks with this method, relapses caused by respiratory acidosis cannot be avoided. We use the technic developed by Laborit, Huguenard, and Alluaume. We avoid the routine application of procaine and procaine amide in view of the frequent occurrence of hypotonia and bradycardia.

In order to facilitate anesthesia, on the evening before the operation, we administer 50 mg. atosil and 200 mg. luminal (phenobarbitol) either orally or intramuscularly. On the day of the operation, the administration of 50 mg. atosil and 25–75 mg. megaphen one and a half to two hours before intubation, and 100 mg. dolantin half an hour before intubation, produces a disinterested sleepy state with clear analgesia from which the patient can still be easily awakened by being spoken to. In infants, the dose of antihistamines and megaphen should be from 0.5 to 1.0 mg./Kg. In cases of controlled respiration following curarization, dolantin may be replaced by pantopon, which has a greater inhibitory effect on respiratory activity. In view of the angioparalysis, the patient should remain in a supine position to avoid untoward blood movement and hypostatic pressure reduction. Except for a temporary acceleration of the pulse rate, which is unpleasant only in rare cases, no disturbances have been observed. This dose only produces minor hypotension, the maximum drop being 10 to 15 mm.Hg.

The dose of barbiturates needed for a reflexless intubation in adults was 150 to 450 mg., the average being 250 mg. The elimination of laryngeal reflexes following this dose was so good that in some cases intubation was possible without succinylcholin, which in other cases was administered in doses of 60 to 80 mg. The doses of barbiturates for children from 3 to 6 years of age were 75 to 100 mg., averaging 80 mg., with simultaneous administration of 20 to 40 mg. succinylcholin. In children from 6 to 12 years of age, the required doses of barbiturates fluctuated from 75 to 150 mg. with an average of 100 mg., while the succinylcholin dose was 40 to 60 mg.

Only small doses of anesthetics are required to maintain anesthesia, because the effect of barbituric acid is not only deepened but also extended. In order to obtain quantitative data, a careful analysis was made of 20 adults and 20 children maintained under anesthesia during one and a half to two and a half hours for pulmonary

resection. In order to maintain anesthesia in 20 children of 3 to 12 years of age, the following drugs were given; 50 to 100 mg. pentothal in 3 cases, 5 to 15 Gm. ether in the closed system in four cases, and no anesthetic drugs in 13 cases. In the 20 adults, the potentiated barbiturate dose had such a prolonged effect that 1:1 N_2O-O_2 in 8 cases, 1:1 N_2O-O_2 supplemented by 10 to 20 Gm. ether in 5 cases, and 5 to 35 Gm. of ether alone in 7 cases were sufficient to maintain anesthetic depth, which was tested by the curare effect at stages II and III_1.

The amount of curare (d-tubocurarin-chloride) required to immobilize the diaphragm and to obtain a nonresistant controlled respiration in adults, was on an average 24 mg. (10 mg. in children). The effect of curare is not appreciably altered by the lytic drug combination. Curare-induced paralysis can be overcome at any time through the administration of prostigmine and atropine.

The dosage indicated to facilitate anesthesia did not completely control but only reduced and delayed the circulatory reactions resulting from hypoxemia and hypercapnia. Compared with potentiated anesthesia, there was a smaller and more delayed fluctuation in the continuous electrophotometric determination of the oxyhemoglobin saturation of the histaminized frontal membrane. The oxyhemoglobin levels in the venous blood were unusually high with the diastolic pressure at such normal levels that appreciable increases of the peripheral flow resistance would be unlikely. The temperatures in the first two hours following the operation were 97.7 F. to 94.1 F. in cases with normal circulatory levels. The fact that the opening of the thorax in a low temperature causes a great loss of heat should be borne in mind. The drop in temperature generally was 97.7 F. to 95.9 F., so that a metabolic decrease of 15 to 25 per cent has to be expected. A total of fifteen blood sugar tests were made at different times within the first two hours following the operation; their results showed values varying from 75 to 131 mg. per cent. In only one patient, whose body temperature was 103 F., did the blood sugar value reach 161 mg. per cent. The blood urea usually only dropped slightly below its initial level. In 25 differential blood pictures, the leukocytosis was found to be 10,000 to 15,000; there also was a lower lymphocyte and eosinophil count.

A deeper vegetative blockage is advisable in extremely serious cases, which normally would not be exposed to any surgical risk. In such cases, preparation for surgery is started one hour earlier and additional quantities of the drugs are injected at intervals into 5 per cent glucose infusion, during the 45 minutes preceding anesthesia. These injections are made away from the vein, in order to avoid thrombophlebitis. Those drugs which are very sour can be successfully diluted in periston. According to the effect obtained, a quantity up to 6 cc. of a mixture of 50 mg. atosil, 50 mg. megaphen, and 100 mg. dolantin is injected. It should be remembered that lytic drugs do not mix with barbiturates. After immediate administration of 2 cc., the additional injections are given—1 cc. every 10 minutes. The patient falls into a deep, analgesic, disinterested sleeplike state, from which he can only be awakened by strong acoustic or mechanical stimuli.

The higher the dosage, the stronger the effect on respiration, bronchial secretion, laryngeal reflexes, pulse rate, and blood pressure. Without an increase of the diastolic pressure, the systolic pressure drops by 15 to 30 mm. Hg. If the patient is left in

cool surroundings, covered only with a sheet, his temperature drops to 97.7 to 95.9 F., suffering a further drop of 0.9 to 1.8 F., during the course of the operation. Under these circumstances, intubation frequently is possible with only 100 to 200 mg. of barbiturates and without a muscle relaxant. During the course of anesthesia, the administration of smaller doses of anesthetics than are needed in mildly potentialized anesthesia becomes necessary. A failure of the lytic combination may occur only in extremely strong persons, for whom larger doses of anesthetics are necessary. Frequently 30 to 50 per cent of nitrogen monoxide or 5 to 15 Gm. of ether are completely sufficient to obtain satisfactory anesthesia. Generally, the bronchial apparatus is so dry that endobronchial aspiration is rarely necessary. In view of the strong angioparalysis, the patient must be kept in a supine position, since changes in position affect the blood pressure. The pulse rate and blood pressure curves become stabilized, while circulatory reactions become understandably indolent and sometimes cease; this is owed to the gas-exchange disturbance and blood losses. Blood should only be replaced in the amount of the loss, and care should be exercised to avoid any possible overtaxing. We infuse at least one-third less than is common practice. The hemorrhagic tendency is slightly reduced in view of the hypotony. According to clinical observation, the danger of effusion also seems to be smaller. If adequate doses of anesthetics are used, the patient can be spoken to at the end of the operation. Vomiting is rare in view of the antiemetic effect of the drugs.

There are no appreciable changes in the postoperative treatment. Oxygen is administered through a nasopharyngal catheter as required. If the patient is returned to bed, the effects of the lytic combination and the analgesics last for an additional three to six hours. The patients will sleep if they are not disturbed. If, however, they are awakened, their psychic and intellectual reactions are normal. Often they remember only the initial intramuscular injection. If the individual is kept in a supine position, both temperature and blood pressure return to normal spontaneously. Sympathomimetics are superfluous and should be avoided in view of possible reactions. If necessary, blood pressure may be altered by changing the patient's position, by administering caffeine, or by injecting strychnine. The motility of the gastrointestinal tract is temporarily slowed or interrupted through the administration of atosil. Megaphen reduces glandular activity. The first feeding, in the form of small quantities of liquids, should take place at the earliest on the evening following the operation.

SUMMARY

The practical application of facilitated anesthesia and of pharmacologic hibernation is described together with the resulting advantages. The suspension of the adrenergic circulatory defenses and the metabolic increase produced by released epinephrine under stress is quite possible. This is not the case with deep general anesthesia. The angioparalytic stabilization of the circulation, the elimination of oxygen-consuming, adrenergic, metabolic reactions, and a temperature-passive

metabolic reduction result in greater safety against respiratory and circulatory hypoxia as well as against shock. The strengthening of the effect of anesthetic drugs makes anesthesia easier. Good respiratory activity without central anesthetic paralysis, postoperative analgesia, desiccation of the bronchial apparatus, and lessening of postoperative complications caused by obstruction atelectasis are undeniable advantages of the method, which also leads to an effective elimination of laryngospastic and bronchospastic complications. Hemorrhages, serohemorrhagic plural effusions, pulmonary edema, and glottic edema are favorably altered or avoided. Not a single contraindication was observed in over 1,000 anesthesias.

BIBLIOGRAPHY

1. Burstein, C. L., et al.: Anesthesiology. *11*:299 (1950); *11*:224 (1950); *12*:411 (1951).
2. Irmer, W., and Koss, F. H.: Grundlinien der Endotrachealen Narkose, Munich, 1951; Zbl. Chir. *77*:129 (1951); Dtsch. Med. Wschr. *78*:361 (1953).
3. Shumacker, H. B., and Hampton, L. J.: J. Thoracic Surg. *21*:48 (1951).
4. Brassfield, C. R., and Gesell, R.: Federation Proc. *1*:10 (1942).
5. Campbell: Abstracts of International Physiological Congress, Copenhagen, 1950.
6. Bolt, W., and Rothkopf, R.: Z. Kreislaufforch. *35*:301 (1943).
7. Gesell, R.; Brassfield, C. R., and Hansen, E. T.: Proc. Soc. Exper. Biol. & Med. *49*:464 (1942).
8. Heymans, C.; Bouckaert, J. J., and Samaan, W.: Arch. internat. de pharmacodyn. et de thérap. *48*:457 (1934).
9. Johnstone, M.: Brit. J. Anaesth. *24*:36 (1952); Brit. Heart J. *12*:239 (1950); Anaesthesia. *6*:138 (1951); Brit. Heart. J. *13*:47 (1951); Brit. M. J. *II*:943 (1951).
10. Nickerson, M., and Brown, H. O.: Anesthesiology. *12*:216 (1951).
11. Schaefer, H.: Plügers Arch. Physiol. *248*:527 (1944).
12. Sloan, H. E.: Surg. etc. *91*:257 (1950).
13. Young, W. G.; Sealy, W. C.; Harris, J., and Botwin, A.: Surg. etc. *93*:51 (1951).
14. Freemann; Schaffer; Schaefer, and Holling: J. Clin. Investigation. *17*:359 (1938).
15. Wiggers; Ingraham; Roemhield, and Goldberg: Am. J. Physiol. *153*:511 (1948).
    Wiggers: Am. J. Physiol. *113*:126 (1945).
16. Remington; Wheeler; Boyd, and Cadell: Proc. Soc. Exper. Biol. & Med. *69*:150 (1948).
    Remington; Hamilton; Boyd; Hamilton, and Cadell: Am. J. Physiol. *161*:116 (1950).
17. Jaulmes, C.; Bénitte, A. C., and Laborit, H.: Compt. rend. Acad. d. sc. 3:372 (1952).
18. Fournel: Compt. rend. Soc. de biol. *146*:561 (1952).
19. Bénitte, A. C.: 20th Session of German Assoc. of Pharmacology, 1953, Bonn.
20. Laborit, H.: Sem. Hôp. 26 No. 69 (1950); Réaction organique à l'agression et choc, Paris, 1952; Anaesthesist. 19, (1952); Presse méd. *60*:573 (1952); Anesth. et analg. *8*:No. 3 (1951); Presse méd. *61*:404 (1953); Acta anaesth. Belg. 2:710 (1951); Bruxelles-méd. 33:863 (1953); 20th Session of German Assoc. of Pharmacology, 1953, Bonn.
    Laborit, H.; Huguenard, P., and Alluaume, R.: Presse méd. *60*:206 (1952).
    Laborit, H., and Leger, L.: Presse méd. *58*:294 (1950).
21. Huguenard, P.: Acta Anaesth. Belg. 2:716 (1951); Anesth. et analg. *8*:5 (1951); 9, No. 2 (1952).
    Huguenard, P., and Mundeleer: Bruxelles-méd. *69*, 1953.
22. Alluaume, R.: Anesth. et analg. *9*:261 (1952).
23. Sénèque, J.: Bull. Acad. nat. méd. *136*:587 (1952).

24. Grosse-Brockhoff, F., and Schoedel, W.: Arch. f. exper. Path. u. Pharmakol. *201*:417 (1943); *201*:443 (1943); *201*:457 (1943).
25. Cremer, H. D.; Kramer, K., and Reichel, H.: Klin. Wchnschr. 23:210 (1944).
26. Brocker, O., and Hell, H.: Tgg. Dtsch. Neurol. u. Psychiatr., Munich, Germany, 1953.
27. van de Walle, J.: Acta anaesthesiol. Belg. *50*:735 (1951).
28. Eichholz, F.; Fleckenstein, A., and Muschaweck, R.: Klin. Wschr. *27*:71 (1949).
29. Zipf, H. F.: Arch. f. exper. Path. u. Pharmakol. *211*:22 (1950). Klin. Wschr., 1953. 20th Session of German Assoc. of Pharmacology, 1953, Bonn.
30. Dews, P. B., and Graham, J. D. P.: Brit. J. Pharmacol. *1*:278 (1946).
31. Levitan, B. A., and Scott, J. H.: Canad. M. A. J. *61*:303 (1949).
32. McCawley, E. L.; Weston, G. A., and David, N. A.: J. Pharmacol. *102*:250 (1951).
33. Cahn, J.; Dubrasquet, and Melon, J. M.: Anesth. et analg. *10*:89 (1953).

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Not every brain operation is followed by serious disturbances; their degree depends greatly on the location of the lesions. With our present knowledge, there can be no doubt that the diencephalic centers and the hypothalamic region are the starting points of these disturbances. Attention is drawn to the experiments performed by Hess,[3] according to whom the hypothalamus is the regulator of all vegetative effectors. This important portion of the diencephalon affects metabolism, temperature, and hemopoiesis, as well as the sleep and waking rhythms, etc.[4] In addition, it maintains close relations (via the thalamus) with the orbitofrontal cortex,[5] with its multiple vegetative links, and its function as the "psycho-vegetative switch."[6] Its further relation with the pituitary gland can also be mentioned. It should be emphasized that the vegetative centers of the spinal bulb form a seat of potential disturbances. For our studies, the substantia reticularis is of great interest as an afferent-efferent converging center.[7]

EXPERIMENTAL FINDINGS

Credit goes to two French investigators for having made valuable contributions on the pathogenesis of the neurosurgical vegetative syndrome, through their experiments in large series of animals. Mosinger[8] produced traumatic, chemical, and physical irritation in the region of the ventricles, involving the hypothalamus, the rhombencephalon, the mesencephalon, the prefrontal area, etc., and found, in accordance with the nature and degree of damage, very acute (or chronic) dysfunctions of the lungs, liver, kidneys, peritoneum, coronary circulation, etc., whose anatomic substrate was similar to the "irritation syndrome" observed by Reilly,[9] when similar splanchnic irritation was present. That syndrome consisted of vasodilatation, endothelial swelling, edema, hemorrhages, infarction, necrosis, and cellular damage.

Tardieu[10] used several agents injected into the third ventricle. He observed thermal disturbances, cerebral edema (especially in the middle region), muscular atony, occasional catatonia and agitation, pulmonary edema, bowel hemorrhages, and renal damage. The injection of minimal doses in the area of the spinal bulb was followed by similar lesions and by serious respiratory changes. Again, from the histologic viewpoint, the characteristic damages of Reilly's syndrome were present.

PATHOGENESIS

Which are the factors which favor vegetative accidents in the field of neurosurgery? The following is partially based on the work of Campan and Lazorthes.[4]

Direct irritation. This can take place in the preoperative stage through the growth of a tumor in the direction of vegetative nuclei. Campan and Lazorthes[4] emphasize

that in such cases there may be an intermediary equilibrium without noticeable symptoms. Sudden changes, such as increased cerebral pressure (hemorrhages in the tumor), diagnostic interventions, and operations, may then lead to an acute vegetative collapse.

The following precipitating factors, among others, must be taken into consideration during surgery: desiccation, cooling, mechanical trauma, direct or indirect pressure, ligature of vessels, and dislocation. Postoperatively the surgical area forms an "irritation center"[4] (autotoxins of the necrotic tissues, hemolytic products and local edema).

Circulatory disturbances. In addition to the mechanical interruptions of the blood supply which become necessary during the course of surgery, the functional circulatory deficiency plays an important role. Even if today we can safely assume that under normal conditions there is no nervous influence on the cerebral vessels, it is possible that damage to the vascular rete (through nervousness) may sensitize it to the point where it will react to normally innocuous irritations with angiospasms.[12] Even an injury of a secondary branch may cause circulatory disturbances in the entire vascular tree area.[13] In addition, there is the possibility of remote damage in other vascular regions, as has been observed in clinical experiments after skull trauma,[14] emboli,[15] inflammatory processes,[16] and similar phenomena. Disturbances of the blood circulation may cause direct damage to the vegetative centers and may result, in the form of secondary effects, in extensive cerebral edema[17] or pressure of the cerebral spinal fluid.[13]

Increased cerebral pressure. In hydrocephalus, we would point out, with Campan and Lazorthes,[4] that the paraventricular nucleus borders directly on the ependyma, and that Roussy and Mosinger[18] have described pressure-sensitive nerve endings in the ventricular walls. This explains the sensitivity of the diencephalon to intraoperative and postoperative pressure fluctuations (air pressure, reactional hypersecretion, and arachnoiditis).

There are many forms of cerebral edema. A perifocal edema enlarges the area of irritation of the tumor as early as the preoperative stage. Moreover, the venous stasis or vegetative irritation may cause a more or less general edema prior to the operation. The acute "active edema," which may be fulminating during the operation and, according to Lebeau,[19] is of neurovasomotor origin, that is, caused by damage to certain areas of the spinal bulb, is especially dangerous. The postoperative cerebral swelling, which may be caused by circulatory disturbances, also produces an extensive vegetative symptomatology. From the pathophysiologic point of view, the cerebral edema is both the cause and the result of a vicious circle (increased cerebral pressure—neurogenic edema—venous stasis—passive edema—respiratory disturbances with hypoxia and hypercapnia—hypertension and increased cerebral circulation—increased cerebral pressure).

In addition to the compression caused by the tumor, each increase of venous pressure in the circulatory system exerts an increasing effect on the cerebral volume and the cerebral spinal pressure. As precipitating causes, unfavorable positions and respiratory disturbances must be considered; in these the oxygen deficiency is of less

significance than the excess of carbon dioxide[20] since only 5 to 7 per cent of CO_2 increases the cerebral circulation by 75 per cent.[21]

Cerebrospinal pressure. This may also be caused by vegetative phenomena similar to those in hypertension. Numerous authorities believe the cause to be reflex[22] and vasospastic[12] factors, perhaps on the basis of a diencephalon lesion.[23, 24]

Vegetative danger is particularly great in operations near the posterior cranial fossa (acoustic neurofibromas, medulloblastomas, cerebella astrocytomas) as well as larger basal meningiomas (suprasellar sphenoid bone, etc.), craniopharyngiomas, pituitary tumors, and pinealomas.

CLINICAL SYMPTOMATOLOGY

The neurovegetative syndrome presents a multiple clinical picture. Of major importance are changes in consciousness, respiratory disturbances, disturbances of the coronary circulatory system, and thermoregulation. Such changes are especially frequent in operations near the diencephalon and the spinal bulb (Vincent et al[25]).

Respiratory disturbances. Polypnea and hyperpnea (rare cases of bradypnea), Cheyne-Stokes or Kussmaul breathing, dyspnea with central pulmonary edema, and rare cases of temporary apnea are observed. All respiratory disturbances must be considered very serious prognostically, since the resulting anoxia and hypercapnia further deteriorate the patient's condition.

Circulatory symptoms. Bradycardia is rare except in cases of severe cerebral pressure; it may be observed alternately with a fast pulse (posterior cranial fossa).[4] Tachycardia is frequent, but should only be given serious consideration when its frequency is high. Increase of blood pressure serves as a sign of cerebral pressure (Cushing's triad) in the preoperative and postoperative stages; during the operation it is occasionally observed in the form of paroxysms, and may even interrupt the favorable drop of blood pressure (author's observation). Together with tachycardia and anhydremia (as expression of increased permeability) it seriously overtaxes the heart. Sudden decrease in blood pressure, without hemorrhage or shock, has been observed, especially in juxtadiencephalic operations.[25] It is often difficult to overcome and its cause may be the retention of blood in the splanchnic region (centralization of the blood circulation) as in the findings of Mossinger and Tardieu.[8, 10] Light vasomotor disturbances of the periphery are therefore quite frequent.

Disturbances of the thermoregulation. Hypothermia is a very rare phenomenon.[26] With greater regularity, central hyperthermia occurs as a consequence of lesions of the calorific center.[23] This is caused by increased heat production[27] and by thermolytic disturbances.[13, 25] Its danger lies in the associated increase of energy requirements and in the vulnerability of the already damaged brain. A temperature increase to 105.8 F. to 107.6 F. is fatal in the majority of cases.

Other disturbances. This category includes symptoms originating in the viscera, such as vomiting, dilatation, stasis, acute hemorrhages, and ulcerations.[5] Polyuria and severe desiccation are signs of dysregulation in the hydrogen exchange. Elevated azotemia following severe albumen catabolism is not infrequent. Spasms and periods of excitement, as symptoms of cerebral irritation, are interesting for our

studies, particularly in view of their effect on metabolism and their increasing effect on oxygen consumption.

NEUROSURGICAL HIBERNATION TECHNIC

In the problem of simultaneous "controlled hypotension," Laborit[45] has criticized the use of ganglion-blocking agents in the face of potential hypoxia. He has instead proposed the use of procaine amide to obtain hypertension. We have taken a stand on several occasions on this problem,[46, 47] and we would not like to dispense with hexamethonium and pendiomid. The effect is excellent, especially in cases of cerebral edema;[48] the increased cerebrospinal pressure is lowered.[49] The use of ganglion-blocking agents is justified by the continuous diastolic retinal arterial pressure,[50] lack of hypoxic EEG changes,[51] severe reduction of cerebral vessel resistance with only slight decrease of cerebral circulation,[52, 53] as well as avoidance of the albumen and liquid loss into the tissues.[54] We have also had favorable experiences with 25 hour long conservative reduction of blood pressure[55] and consider controlled hypotension as a circulatory equivalent of hibernation. In addition, the hibernation serves as a defense against possible hypoxia following strong hypotension. The suppression of vegetative impulses in the periphery by ganglion-blocking agents is also very desirable. We agree with Schneider[12] that a mean blood pressure of 50 mm.Hg. should be considered as a routine minimal hypotensive level; however, according to animal experiments[12] temporary lower levels are absolutely acceptable.

On the question of the "optimal hypothermia" of the brain, the experiments conducted by the school of Schneider[12] show that cooling under 93.2 F. seems to be useless, since that level is the most favorable for recovery after ischemia; the vulnerability becomes greater under 87.8 F. In addition, Lazorthes and Campan[56] state that a hypothermia under 93.2 F. (minimum of 86 F.) has an effect which surpasses that of the purely pharmacologic hibernation, since it appears that only then a complete inhibition of the pituitary is obtained.[57] It also should be mentioned that the cortical function ceases at temperatures under 87.8 F.,[57] making additional anesthesia superfluous. Thus, one is led to resort to a great lowering of the temperature in serious cases, bearing in mind, however, that this makes "the way back" more difficult.

Preoperative findings stress: cardiopulmonary findings, EKG, nonprotein nitrogen, renal concentration test, coagulation status (coagulation time, prothrombin index, secondary hemorrhage time, thrombin count). The coagulation status in many cases reveals changes associated with a greater hemorrhagic tendency. The preparation for surgery consists of the administration of high doses of vitamins P, C, and K, one or two days prior to the operation, with the customary premedication of potentiated anesthesia.

Half an hour before the operation, start a glucose infusion (5 per cent) with 4 Gm. of novocain/1,000 cc.; inject intravenously every 10 minutes 1 cc. of the M_1 mixture (largactil, phenergan, and dolantin). Carry out endotracheal intubation with 0.5 Gm. pentothal and succinylcholin; place patient in inclined position (approximately 30°). Reduce blood pressure with small doses (20 to 50 mg.) of pendiomid, until

systolic levels of approximately 70 mm.Hg. are reached. We use arfonad (thiophanium in doses of 0.5/1 cc. of infusion solution) in cases where a short controlled hypotension, to last only for the time of the operation, is desired.

The anesthesia, with nitrous oxide and oxygen in a proportion of 3–2:1, is continued until opening of the dura, at which point oxygen is administered. Through manipulations at pain-sensitive sites (meningea media, basal meninges, tentorium) desensitivity should be increased with intravenous administration of 0.5 to 1 cc. of M_1. The same procedure is adopted in case of fluctuations in pulse and respiration rates. Blood pressure is maintained at stable levels through the administration of additional ganglion-blocking agents.

Caution is advisable in the dosages of ganglion-blocking agents since strong potentiation of their effects, as well as increased requirements during hibernation, have been described[58] (also see the discussion of this question in Anesth. et analg. *10*:326–328, 1953). We are under the general impression that an improved stability of the blood pressure level is obtained.

Following the horizontal position during the operation, systolic pressure should increase to 80 to 90 mm.Hg. In the postoperative stage, the patient is covered only with a sheet and receives for 2 to 3 days 0.3 Gm. pyramidon rectally, 50 mg. pendiomid[6] intramuscularly every 4 hours, and divided intramuscular doses of M_1 as required. Pulse rates should be 90 to 110 per minute, systolic pressure 80 to 100 mm.Hg., respiratory rate 8 to 10 a minute, and temperature 93.2 F. to 96.8 F.

Several German researchers also employ similar technics.[12, 58, 59] Campan and Lazorthes[4] favor a much slower induction (one and a half to three hours). As to the cooling, we believe that the temperature drop to 93.2 F. to 95 F. obtained with the lytic mixture M_1 is sufficient in almost every case; however, the hibernation should be deepened without delay in case of persistent vegetative disturbances. When the temperature is lowered, it is important to wait until deep sleep and adequate blocking is obtained before starting the application of ice packs. It is equally important to assure an even drop of the temperature curve. We do not believe that an intubation in local anesthesia, advocated by some researchers,[56, 21] is necessary, since a favorable respiration of short duration is all that is necessary under succinylcholin, and the anesthesia is usually sufficient to avoid coughing and straining.

Difficulties in reducing the blood pressure can be overcome by changing the preparation and by administration of hydergin, regitin or procaine amide. In case of hypersensitivity to one of the components of the lytic mixture, especially dolantin, that component is replaced by another drug (nembutal, chloral rectally, etc.). Some authors recommend diparcol in view of its stimulatory effect on the respiration, particularly in secondary bronchorrhea caused by phenergan.[4, 60]

Postoperatively, the patient should generally regain his reactivity and ability to swallow after 12 to 18 hours, even if a state of mild somnolence persists. In spite of this, the temperature should not rise above 96.8 F. (awake hibernation[56]). We consider of particular importance a gradual rise in blood pressure during the first day, for which we resort to the continuous administration of angioparalytic agents and thereby combat simultaneously postoperative cerebral edema. Very low doses

are necessary for children, the same being true in people of advanced age in whom the duration of hibernation should be kept to a minimum.

At the end of hibernation, if definite symptoms of the neurovegetative syndrome appear, hibernation should then be deepened for approximately another 24 hours. However, one should be careful to obtain a balance of the neurologic status at regular intervals. The duration of the hibernotherapy cannot be inflexibly determined, but must be adapted to the clinical picture; Campan and Lazorthes[4] continued hibernotherapy in one case for a full month, to the best of our knowledge the longest period on record.

RECENT EXPERIENCE

Respiratory disturbances are rare, even during manipulation of the pons or the medulla oblongata. They are almost absent during the postoperative stages. The blood pressure level remains remarkably stable, and the loss of blood is tolerated without any sign of shock. There are a few cases of resistant tachycardia which can only be overcome by very deep hibernation.[4] In the great majority of cases, the pulse rate is only slightly accelerated. Pampus[13] was able to control rapidly an arrhythmia with largactil, during an operation for a hypophyseal tumor.

Hyperthermia can be avoided with few exceptions. In those cases, only cryotherapy becomes necessary sporadically, since pyramidon reinforces the temperature drop produced by largactil.[62] Loew[58] recommends the intravenous administration of novocain to increase the temperature.

Cerebral vomiting, singultus, and similar phenomena are practically nonexistent. The spasmodic tendency of the brain is further decreased.[13] (David et al[60] emphasize the beneficial effects of largactil when used with novocain in cases of status epilepticus.) States of excitement and motor unrest, which are sometimes seen after frontal and temporal lobotomies and hypophyseal interventions, did not occur.[13]

Indication for hibernation. Hibernation appears to be mostly indicated in:[4, 13, 60] (1) operations in the area of the diencephalon (tumors of the third ventricle, craniopharyngiomas, pinealomas, olfactory, sphenoid, and suprasellar meningiomas); (2) operations in the area of the posterior cranial fossa (tumors of the fourth ventricle, especially in children, and of the cerebellum and the cerebellopontile angle); (3) revulsive hydrocephalus operations in children; (4) total extirpation of large tumors, accompanied by acute decompression, lobectomies, and hemispherectomies; (5) highly located cervical tumors (no respiratory disturbances).

In addition, pharmacologic hibernation is recommended in cortiseptomy under corticographic control, that is, without barbiturates, so as to permit neurologic interpretation.[60] It is further recommended in stereotropic operations.[67]

Hypophyseal tumors are a contradictory subject. On the one hand, Hell[68] observed severe postoperative hyperthermia, which could not be altered by deep hibernation, and on the other hand, David et al[60] as well as Kuhlendahl[69] emphasize the extreme sensitivity of these cases, even after pretreatment with hormones.

With reference to conservative hibernotherapy, we would like to issue a strong warning that it should only be resorted to (perhaps with the exception of hypo-

physeal tumors) in cases of severe postoperative disturbances, since it is mostly ineffective.[59] In all dangerous operations, the hibernation therapy should be routinely started before the initiation of surgery.

A promising field of application seems to be in meningitis and encephalitis.[13, 70] The possibilities in disturbances of cerebral circulation seem rather doubtful to us. The experiences with severe trauma of the cranium with involvement of the spinal bulb are very limited, not permitting a final conclusion. Tourain[71] had rather unfavorable results. In this field, the most recent report from Woringer et al[38] is of great interest. These researchers chose 19 cases which were, according to their criteria, completely hopeless, they saved 3 of them. Eleven improved temporarily (regaining of consciousness and the swallowing reflex and improvement of hyperthermia and hyperventilation). The histopathologic examination of 12 patients revealed typical hemorrhages of the spinal bulb and signs of glial reaction, that were taken as indications of initial regeneration after prolonged hibernation. It therefore seems that an attempt with this method is worth while in desperate cases.

Personal results. Our surgical experiences are based upon 45 cases made up almost entirely from indication group one and some belonging to group two including three tumors of the third ventricle, a medulloblastoma of the fourth ventricle, a large cranial pharyngioma, a bilateral acoustic neurofibroma, and 4 relapsed acoustic neurofibromas with partially severe bulbar symptoms. The remainder included cases of large basal meningiomas, tumors of the cerebellopontile angle, and basal aneurisms. We lost 7 patients of this group—4 cases of softening (after localization or expansion not compatible with life), 1 inoperable cholesteatoma, and 2 undiagnosed secondary hemorrhages.

In all other cases, the intraoperative and postoperative course was of a benign nature never before observed. Our results must be considered highly encouraging in view of the seriousness of the cases treated. More than anything else, it seems possible to enlarge considerably the indication for radical operations.

Disadvantages and dangers. In favorable hibernation, the symptoms of secondary hemorrhages may be greatly masked or even fully absent.[13, 58] The supplementary ganglion-blockage sometimes eliminates the most constantly appreciable symptom, namely, the increase of blood pressure. Therefore, it is advisable to make the hibernation superficial as early as possible to permit timely diagnosis of clouding of consciousness, changes in pulse rate, blood pressure, and respiration.

A further disadvantage is the difficulty of determining neurologic sequelae to the operation, because strong reduction of the reflexes and lateral differences of the motoricity cannot be easily appraised. In such cases, "undulating hibernation" is advisable. Another danger lies in the form of the hypersensitivity of those cases with possible irreversible hypothermia. We have already discussed the hypophyseal tumors, and the same is true for many skull traumas;[56] cases with operative interruption of the arterior cerebri anterior may also react abnormally.[60] Campan and Lazorthes[4] consider this a diencephalic hypophyseal insufficiency. The resistance to hibernation as an untoward reaction is quite strong in a few cases.

Finally, attention must be directed to the observations of Lazorthes and Campan,[56]

which include chronic, possibly fatal sequelae on the basis of a "diencephalitis" (anorexia, cachexia, trophic disturbances). These authors consider this a new syndrome in patients who would not have survived the operation without hibernation. Thus, a new outlook on a completely new problem is encountered.

SUMMARY

A review of the acute neurovegetative syndrome during and after neurosurgery is presented, including the analysis of results of pharmacologic and clinical experiments on the limits of "artificial hibernation" in brain surgery. It is concluded that this method is important in neurosurgical anesthesia. The reduction of vital activity allows the patient to be carried over a dangerous time span in the state of "narcobiosis,"[72] possibly extending the limits of surgery.

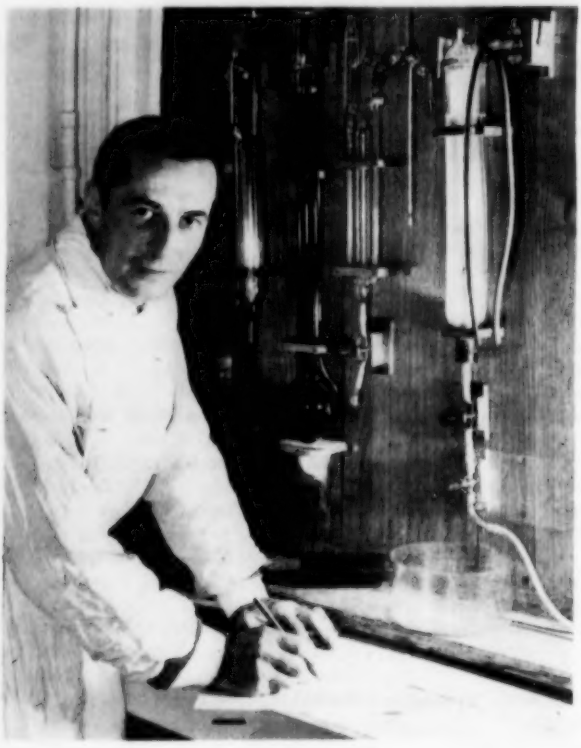
BIBLIOGRAPHY

1. Lazorthes, G., and Campan, L.: Presse méd. p. 645, 1952.
2. Tardieu, G., and Tardieu, C.: Le système neurovégétatif, Paris, Masson, 1948.
3. Hess, W. R.: Das Zwischenhirn, Basel, Schwabe, 1949.
4. Campan, L., and Lazorthes, G.: in Laborit's and Huguenard's "Pratique de l'hibernothérapie," Paris, Masson, 1954.
5. Krauland-Steinbereithner, F.: Wien. Arch. Psychol. Psychiatr. Neurol., Jan. 3, 1953.
6. Hopf, H.: Wien. Klin. Wochenschr. *75*:157, 1951.
7. Magoun, H. W.: Physiol. Rev. *30*:459, 1950.
8. Mosinger, M.: Médecine pathogénique et cancer, Paris, Masson, 1952.
9. Reilly, J.; Rivalier, E.; Compagnon, A., and Lapeane, R.: C. R. Soc. Biol., 116, 24, 1934.
10. Tardieu, G.: Le coma, Thèse de Paris, 1942.
11. Wanke, R.: Langenb. Arch. Dtsch. Zeitschr. Chir. *270*:386, 1951.
12. Schneider, M.: Langenb. Arch. Dtsch. Zeitschr. Chir. *276*:23, 1953.
13. Pampus, F.: Chirurg *24*:298, 1953.
14. Schneider, M.: Dtsch. Zeitschr. Nervenheilk. *162*:113, 1950.
15. Villaret, M., and Cachera, C.: Les embolies cérébrales, Paris, Masson, 1939.
16. Schallock: ibid 13.
17. Spatz, H.: Zeitschr. Neurol. *167*:301, 1939.
18. Roussy, L., and Mosinger, M.: Traité de neuro-endocrinologie, Paris, Masson, 1947.
19. Lebeau, J.: Rev. canad. biol. *7*:402, 1948.
20. Bodechtel, G.: Verh. Dtsch. Ges. Kreisl. Forschung. *19*:109, 1953.
21. Vourch, G.: Cahiers d'Anésth. No. 6, 33, 1953.
22. Huber, K.: Arch. f. klin. Chir. *200*:65, 1940.
23. Kraus, H.: Wien. Klin. Wochenschr. 1950.
24. Chorobsky, J.: J. Neurol., Neurosurg., & Psychiat. *13*:28, 1950.
25. Vincent, C.: Proc. Roy. Soc. Med. *40*:689, 1947.
26. Brun, M.: Les soins et les suites opératoires en neurochirurgie, Thése de Paris, 1944.
27. Dott, C.: Ibid. 4.
28. Vichnewsky: Ibid. 4.
29. Angel, J. M.: La thérapeutique par le sommeil, Paris, Masson, 1953.
30. Fay, T.: New York State J. Med. *40*:1351, 1940.
31. Zipf: 20th Session of German Assoc. of Pharmacology, Oct. 4–7, 1953, Bonn.
32. Courvoisier, S.; Fournel, J.; Ducrot, R.; Kolsky, M., and Koetschet, P.: Arch. internat. de pharmacodyn. et de thérap. *92*:305, 1952.
33. Weise, H.: 20th Session of German Assoc. of Pharmacology, Oct. 4–7, 1953, Bonn.
34. Peruzzo, L., and Forni, R. B.: Minerva anestesiol. *9*:1, 1953.

35. Hunkel: Ibid. 13.
36. Bovet, D.: Anaesthesist. 3:13, 1954.
37. Terzian, H.: Rass. neurol. veget. 211, 1952.
38. Woringer, E.; Schneider, J.; Baumgartner, J., and Thomalske, G.: Anesth. et analg. *11*:34, 1954.
38a. Aron, E. et al.: Ibid. 38.
39. Halpern, B., and Cruchaud, S.: C. R. Soc. Biol. Paris, 622, 1948.
40. Eichholtz, F.: Klin. Wochenschr. *761*:1950.
41. Fleckenstein, A.: Anaesthesist. 3:15, 1954.
42. Borré, L. A.: Anaesthesist. 3:6, 1954.
43. Shanes, A. M.: J. Gen. Physiol. 33:57, 1949.
44. Huguenard, P.: Anaesthesist. 2:33, 1953.
45. Laborit, H.: Anesth. et analg. *9*, No. 3, 1952.
46. Kucher, R., and Steinbereithner, K.: Anaesthesist. 2:167, 1953.
47. Kucher, R., and Steinbereithner, K.: Anaesthesist. 3:47, 1954.
48. Bein, H. J., and Meier, R.: Anaesthesist. 3:25, 1954.
49. Sack, H., and Handrick, H. G.: Medizinische. *1*:375, 1952.
50. Kucher, R., and Steinbereithner, K.: Anaesthesist. 2:68, 1953.
51. Guiot, G.: Ciba Symposium. *1*:185, 1954.
52. Bernsmeier, A.: Verh. Dtsch. Geselsch. innere Med. 411, 1953.
53. Crumpton, C. W., and Murphy, Q. R.: J. Clin. Investigation. *31*:622, 1952.
54. Kölbl, H. R.; Kucher, R., and Steinbereithner, K.: Anaesthesist. 3:56, 1954.
55. Schönbauer, L.; Kucher, R., and Steinbereithner, K.: Wien. Med. Wochenschr. 185, 1953.
56. Lazorthes, G., and Campan, L.: Anesth. et analg. *11*:1, 1954.
57. Cahn, J.: in Laborit and Huguenard's "Pratique de l'hibernothérapie," Paris, Masson, 1954.
57a. Dogliotti, A. M., and Ciocatto, E.: Schweiz. med. Wchnschr. 707, 1953.
58. Loew, F.: Langenb. Arch. Dtsch. Zeitschr. Chir. *276*:702, 1953.
59. Röttgen, P.: Kongr. Gesellsch. Dtsch. Neurologen und Psychiatr., August 26–29, 1953, Munich, Germany.
60. David, M.; Talairach, J., and Deligné, P.: Soc. Neurochir. Langue Franç. Dec. 2, 1953.
61. Huguenard, P.: Cahiers d'Anésth. No. 6, 9, 1953.
62. Friebel: 20th Session of German Assoc. of Pharmacology, Oct. 4–7, 1953, Bonn.
63. Pampus, F.: Langenb. Arch. Dtsch. Zeitschr. Chir. *276*:708, 1953.
64. Woringer, E.; Schneider, J.; Brogly, G., and Baumgartner, J.: Rev. Neurol. *87*:515, 1952.
65. Steinbereithner, K.: Wien. klin. Wchnschr. (in press).
66. Kucher, R., and Steinbereithner, K.: Anaesthesist. 2:196, 1953.
67. Zysno: Kongr. Gesellsch. Dtsch. Neurol. und Psychiatr., August 26–29, 1953, Munich, Germany.
68. Hell: Ibid. 67.
69. Kuhlendahl: Ibid. 67.
70. David, G.: in Laborit and Huguenard's "Pratique de l'hibernothérapie," Paris, Masson, 1954.
71. Tourain, Y.: Presse méd. 470, 1953.
72. Decourt, P.: Rev. Path. Gén. 53:1560, 1953.

about the guest editor

Doctor Henri Laborit was born on November 12, 1914, in Hanoi, Indochina, where his father was on duty in the Army Medical Corps. In 1933, he entered the Ecole Principale du Service de Sante de la Mare et des Colonies in Bordeaux, France, and he was graduated from this institution in 1938. He had been appointed internist of the Bordeaux hospitals in 1936. After the outbreak of the war, he served as surgeon on the battleship, "Sirocco," which fought gallantly at Dunkirk. During the remainder of the war, Dr. Laborit served with the Free French Navy Forces, and in 1942, he was surgeon at the Dakar hospital. In 1944, he was appointed surgeon of the aircraft carrier, "Emile Bertin," which participated in the landings in Anzio and in Southern France.



HENRI LABORIT, M.D.

Doctor Laborit began his research on the neurovegetative system and chemical nervous mediators when he was assistant surgeon at the Naval hospital of Toulon during 1944 to 1946. From the end of 1946 to 1948, he served as a surgeon on naval hospital ships in Indochina. He was appointed surgeon of the naval hospital of Lorient. During this period, Dr. Laborit carried on his research on shock and introduced synthetic curares in war surgery. In 1949, he was appointed surgeon of the navy hospital of Bizerte. At this time he developed the potentiated anesthesia and continued his work on organic reaction to stress and shock.

Since 1951, Dr. Laborit has been at the Centre de Recherches de l'Armee at the military hospital, Val de Grace, in Paris. He directs and supervises the experimental and clinical research on artificial hibernation. In Paris, Dr. Laborit works with Professors Lacomme, Seneque, and Jean Gosset, and he also is associated with Colonel Chippaux, army surgeon, who supervises the application of artificial hibernation to war surgery in Indochina. Under the leadership of Dr. Laborit, research on artificial hibernation has also been started in Germany, Austria, Switzerland, Italy, Belgium, and Holland.

Doctor Laborit is the author of innumerable papers on the subject of artificial hibernation and has also written the books, *Physiologie et Biologie du Systeme Nerveux Vegetatif*, which received an award from the French Academy of Medicine, and *L'Anesthesie Facilitée par Les Synergies Medicamenteuses*.

GENERAL PRACTICE CLINICS

This new monthly section of General Practice Clinics features reports of papers delivered at current medical meetings in the United States and abroad.

Recognition and Management of Diseases of the Pancreas

Presented by C. WILMER WIRTS, M.D., (Jefferson Hospital, Philadelphia, Pa.) before the 18th annual Postgraduate Institute and Convention, Philadelphia County Medical Society, Philadelphia, March 30–April 2, 1954.

In general, diseases of the pancreas can be divided into three categories: congenital, inflammatory, and neoplastic. Of these, acute and chronic pancreatitis and carcinoma of the pancreas were discussed.

Acute pancreatitis is characterized by the sudden onset of severe abdominal pain radiating into the back and often progressing into shock. Differential diagnosis includes consideration of perforated viscus, intestinal obstruction, biliary and ureteral colic, mesenteric thrombosis, coronary occlusion, and, in the female, ruptured ectopic pregnancy. An elevated serum amylase is almost pathognomonic.

Other informative laboratory studies include those which will determine the presence of hyperglycemia, hyperbilirubinemia, acidosis and, after 24 to 72 hours, hypocalcemia. X-rays of the abdomen will often reveal air under the diaphragm, distension of the small bowel or calcification in the pancreas, the biliary tract or the urinary tract. Urinalysis is important to detect hematuria often present with renal stone.

Good surgical judgment today dictates that these patients be treated conservatively unless they fail to respond. Conservative treatment consists of: relief of severe pain with morphine or an allied drug. "The spasmogenic effect is outweighed by the relief provided—use it!" Later, after the pain has subsided somewhat, phenobarbital can be used. Anticholinergic drugs can be used but have their side effects and should be used with care. Lower blood Cl and K are usually present and these should be given intravenously along with glucose. In severe shock blood transfusions are important. Crysticillin and streptomycin are used every 12 hours after admission, with further usage guided by results. Gastric suction and aluminum hydroxide may be used to overcome nausea. After 24 to 72 hours, a response should be noticeable. When the response is noticeable, treatment can be stopped. If not, a complication such as cyst or abscess is usually present, and surgery is necessary. Surgery is indicated for complications and is elective after convalescence for associated disease, particularly of the biliary tract.

Chronic relapsing pancreatitis is a disease that is often wrongly diagnosed and the physician must be alert to the possibility. It is characterized by recurrent bouts of abdominal pain, usually in the epigastric region radiating through to the back. There is a paucity of physical findings. Cachexia and a multiple scarred abdomen are often present. This is due to the frequent removal of normal gallbladders and appendices in an attempt to relieve the pain. Transient bouts of hyperbilirubinemia, hyperglycemia, glycosuria and increased urine urinobilinogen are significant findings. Creatorrhea and steatorrhea should always be searched for since they are indicative of advanced pancreatic insufficiency. Trypsin and bile flow tests are also helpful. The secretin test can now be made, since normal and abnormal values have been established. However, this test is too cumbersome, time consuming, and expensive to be of great general use. Today, in addition to relieving pain, treatment is usually directed towards correcting reflux or back pressure in the main pancreatic ducts.

Carcinoma of the pancreas is the third most frequent site of malignancy of the gastrointestinal system. The earliest symptom is weight loss, followed by moderate to severe epigastric pain radiating through to the back and, finally, the development of progressive jaundice. When the lesion is located in the body or tail, jaundice may not be present. Again alertness to the possibility of this lesion is important. Of the many pancreatic function tests described probably the most important is the examination of the stool for abnormal amounts of fat or undigested meat fibers. Roentgen study is rarely of much help in diagnosis. Biochemical studies of the blood and a determination of the enzyme content of duodenal aspirates is of additional aid in evaluating these cases. Confirmation of the diagnosis requires surgical intervention and histologic study. In a few instances in which the diagnosis of carcinoma of the pancreas is made early, resection of the lesion, particularly when it involves the body or tail, may be practical. However, when the head of the pancreas is involved a palliative procedure to relieve biliary obstruction is now generally considered the treatment of choice.

Respiratory Failure of the Newborn

Presented by JAMES L. WILSON, M.D., (University Hospital, Ann Arbor, Michigan) before the Eighth Annual Michigan Clinical Institute, Detroit, Michigan, March 11, 1954.

In the latter half of fetal life, rhythmic, but discontinuous, respirations do occur. The factors which control respiration have been active before birth, and respiratory activity is continued after birth only under different circumstances. There is still a great deal to be learned about the transport of oxygen by the fetal blood and also about the resistance to anoxia possessed by the newborn. When a child

is not breathing, it is useless to set any gas mixture flowing across his nose and mouth. Furthermore, respirators are effective only when there are no respiratory movements being initiated by the infant and when the airway is clear. To use an artificial respirator to correct atalectasis requires more pressure than can safely be allowed. Lung rupture occurs due to lack of lung expansion, diminished amount of active lung, or excessive pressure. Pneumothorax may occur through misuse of this equipment. Some form of mouth to mouth breathing is often best. Risk of some damage to the lungs may be necessary to save life. The important object is to follow the respiratory rhythm initiated by the infant's center and aid any movements resulting from this rhythm. The Drinker and positive pressure respirators have are faulty in that they resist natural movements of the infant and establish their own rhythm. A mask is still the best readily available system and is more desirable than the Drinker device. Laryngospasm, as well as other smooth muscle contraction, sharply reduces the effectiveness of these devices. Slight glottus spasm can prevent respiration despite considerable pressure.

Anesthesia in Operative Obstetrics

Presented by PERRY P. VOLPITTO, M.D., (Professor of Anesthesiology, Medical College of Georgia; Director of Anesthesia, University Hospital, Augusta, Georgia,) before the 17th Annual Meeting of the New Orleans Graduate Medical Assembly, New Orleans, Louisiana, March 8–11, 1954.

Doctor Volpitto discussed the use of inhalation anesthetic agents. One must bear in mind that he is dealing with anesthetic agents that can and do affect not only the mother and fetus, but may also interfere with the mechanism of labor. Hypoxia is always a possibility with either nitrous oxide or ethylene and, therefore, one must use a mixture containing at least 20 per cent oxygen.

Trichlorethylene seems to work well in some instances and not in others. The best use for this agent in obstetrics seems to be as an analgesic in the first stage; it does not seem as useful in the second stage and should not be used during the actual delivery for total anesthesia. Demerol given in 50 to 75 mg. amounts beforehand enhances the value of trichlorethylene in the first stage of labor.

The difficulty with the use of inhalation anesthetics during the first stage was the necessity of another person being with the patient. This poses a personal and financial problem when this stage is prolonged.

Vinethene was described as a useful agent. However, Dr. Volpitto stated that there were disadvantages in that during the warm summer months the agent tended to be too volatile unless used in a cool room. Also, he had found that there was a tendency for the mechanism of labor to be interfered with if anesthesia

superseded analgesia. Dr. Volpitto discussed the effects of these agents on the fetus. When the inhalation anesthetics are being used to produce analgesia only, they have little effect upon the fetus. But when they are used in sufficient amount to produce a definite anesthesia, they have a tendency to produce fetal respiratory depression.

Operative obstetrics proper was then discussed under the following headings:

Dystocia dystrophy. Dr. Volpitto stated that it was useful to administer morphine sulfate to these patients to produce a situation where the uterus might relax better between the contractions. Inhalation anesthetics are useful with these patients, but he mentioned the drawback that if the labor has gone on for more than 24 hours there may already be a fetus in distress, which will be further depressed with the use of these agents. Dr. Volpitto liked to use low spinals with these patients, rather than an inhalation anesthetic. He stated, however, that one must always be prepared for the possibility of the patient going into hypotension. Since the pressure of the gravid uterus interfered with venous return to the right heart, these patients are particularly prone to go into a hypotensive state with low spinal anesthesia.

Uterine contraction rings. In this condition Dr. Volpitto said that regional anesthesia is of no value. One needs to produce a deep anesthesia to relax the uterus; the agent of choice here is ether. Chloroform produces the necessary depth of anesthesia only at a level that is dangerous to the mother and, therefore, should be avoided in these cases.

Toxemia and eclampsia. The problem in these patients is that they are very ill, hypertensive, and may be very close to or actually convulsing. In these cases, particularly, proper treatment of the problem involved is necessary. One should not be in a hurry to do an operative procedure. One should give oxygen to the mother in an attempt to oxygenate the fetus. For cesarean section in these cases, regional anesthesia (spinal or caudal), or even local anesthesia, is the method of choice. However, Dr. Volpitto found that in his experience it is difficult to get the average patient to accept spinal anesthesia for a cesarean section. He stated that one has the danger of a blood pressure drop occurring, but in the case of a severe toxemic, or an eclamptic, this is not as serious as it might seem at first. He states that in these cases he will allow the blood pressure to drop a third of normal. If it falls further, vasopressor drugs may be used to raise it to about a level where the decrease is only 15 to 20 per cent or normal for the patient.

Premature separation of the placenta. Dr. Volpitto stated that here the inhalation anesthetics are the agents of choice, the best being cyclopropane. He went on to say that "in the best of hands, 35 per cent to 40 per cent of infants are apneic at birth with inhalation analgesia. The need for adequate facilities and ability to resuscitate the newborn is self evident."

Placenta previa. Dr. Volpitto emphasized that here one should be especially concerned about any blood pressure drop that might occur with a spinal anesthetic.

Version and extraction. One needs a very deep anesthesia so that there will be sufficient uterine relaxation to avoid the possibility of a uterine tear. Inhalation

anesthetic agents should be employed, preferably ether. Tubocurarine or its substitutes are of no value here as they only relax skeletal muscles.

Cesarean section. Dr. Volpitto emphasized again that with the use of inhalation anesthesia one will always have a high percentage of apneic babies. He stated that the same thing will occur with the use of pentothal anesthesia. He showed slides to illustrate the point that if the baby is delivered within 10 minutes or less after the anesthesia is started, there is little depression. But the curve of incidence of depression of the fetus rises rapidly after this point. This fact was used as a basis for the recommendation that regional anesthesia was to be preferred whenever one suspected that the operative procedure would be rather lengthy before delivery of the baby. Dr. Volpitto went on to say that whatever applied to anesthetic rules for cesarean section also applied to forceps, but that here one also added the problem of producing sufficient muscle relaxation. Tubocurarine chloride or its substitutes are of value here.

Dr. Volpitto said that he does not use preanesthetic barbiturates, and on the morning of surgery, the mother is usually given 50 mg. of demerol and 0.4 scopolamine, 60 to 90 minutes prior to surgery. He stated that "the longer the procedure, the deeper the anesthesia, and the greater the need may be for resuscitation of the newborn."

The final conclusion was given as follows: "Use the anesthetic agent and technic you have had the most experience with."

THE JOURNAL OF CLINICAL AND EXPERIMENTAL PSYCHOPATHOLOGY AND THE QUARTERLY REVIEW OF PSYCHIATRY AND NEUROLOGY will publish the following in the July–September 1954 issue:

A SYMPOSIUM ON
SOMATOTHERAPIES IN PSYCHIATRY

with these contributors writing on the following subjects:

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INCORPORATING INTERNATIONAL RECORD OF OPHTHALMOLOGY

FOREWORD

The objective of the QUARTERLY REVIEW OF OPHTHALMOLOGY is to bring together in one publication concise but authoritative abstracts of current articles on ophthalmology, according to an all inclusive plan which includes all special, state, and national journals as well as the bulletins of clinics, hospitals, etc., and the transactions of meetings. This embraces both the domestic and foreign literature.

To assist the reader to locate quickly the articles of current interest all data are classified and published according to the following systematic plan:

Anatomy, Embryology, Heredity, Development and Nutrition

Optics, Physiology and Psychology of Vision

Physiology, Chemistry and Biochemistry of the Eye

Pathology, Bacteriology and Immunology

Diagnostic Methods of Examination Biomicroscopy and Photography

Ocular Movements and Motor Anomalies, Nystagmus, Reading Disability

Anomalies of Refraction and Accommodation, Contact Lenses

Conjunctiva

Cornea, Sclera and Tenon's Capsule

Anterior Chamber and Pupil

Uveal Tract and Sympathetic Ophthalmitis

Crystalline Lens

Vitreous Humor

Retina

Neuro-Ophthalmology, Optic Nerve, Visual Pathways, Centers and Visual Fields

Eyeballs, Exophthalmos and Enophthalmos

Glaucoma and Hypotony

Lacrimal Apparatus

Eyelids

Orbit

Allergy

Anesthesia

Medical Ophthalmology

Pharmacology, Toxicology and Therapeutics

Comparative Ophthalmology

Tropical Ophthalmology

Hygiene, Prophylaxis, Occupational Ophthalmology and Injuries

Illumination and Illuminating Engineering

Ophthalmic Sociology

Education, History and Institutions

Miscellaneous

Book Reviews

Announcements

A section entitled International Record of Ophthalmology is included at the beginning of the journal. The Record Section consists of advanced clinical and experimental reports.

Quarterly Review of **OPHTHALMOLOGY**

The Role of Vision in Motor Vehicle Operation

A REVIEW*

Leon Brody, Ph.D.†

NEW YORK, N. Y.

It is generally accepted that adequate vision is essential to the safe operation of a motor vehicle. Yet statistical research seems to show little significant relationship, and often none at all, between drivers' visual abilities and their records of safety on the road. This rather startling discrepancy is not too difficult to explain. However, there are other pertinent questions of a more complex nature that need to be answered before the full role of vision is known and benefits are reaped from this knowledge. Specifically: What constitutes adequate vision for the job of driving a car? How is a driver's vision affected by external and internal variables? What can be done to improve vision examinations for driver licensing? How can visual *performance* in driving be improved?

VISUAL ABILITIES AND ACCIDENT RECORDS

Many more studies have been made of the relation between visual abilities and accident records than could possibly be mentioned here. However, a sampling of the more important investigations is revealing. Here are some of the highlights:

(1) A large battery of tests was administered to over 3,000 drivers in the state of Connecticut. Correlations with accident records were reported for 28 variables concerned with visual sensation and perception, including visual acuity, field of vision, resistance to glare, and depth perception. The findings: only a very slight relation to an over-all accident index. Efforts to relate specific visual factors to the occurrence of specific types of accidents (for example, relating glare resistance measures to night accidents) produced essentially negative results.[7]

(2) Some 2,000 persons in the District of Columbia were tested for visual acuity, glare sensitivity, color vision, and speed estimation, and their test scores were correlated with arrest and accident data for a period of years both preceding and subsequent to the testing program. The correlations obtained were all very low; in fact, none differed significantly from zero.[8]

(3) In a study of Michigan drivers, comparing accident repeaters and accident-free drivers who were matched for age, sex, and driving experience, the accident-free group was found to be significantly better on acuity, depth perception, and muscle balance. No significant differences were found with regard to field of vision or rate of dark adaptation.[10]

(4) Since the fall of 1952 the Center for Safety Education has been cooperating with the New Jersey Division of Motor Vehicles in an Accident Prevention Clinic for the examination of accident repeaters

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* This article is based on a paper presented at the First Occupational Vision Conference, which was sponsored by the University of Maryland and cooperating agencies, on March 3, 1954, in Baltimore, Maryland.

† Director of Research and Publications, Center for Safety Education, New York University.

and chronic violators. Preliminary findings for 947 violators make it seem unlikely that poor field of vision, poor visual acuity, or color blindness will distinguish these violators from drivers who have good records. Results with tests of glare recovery and depth perception suggest that improved tests are very much needed.

Many other studies could be mentioned,* but it is generally apparent that the relationship between measures of vision and records of accidents is of small significance in some respects and practically negligible in others. There are a number of reasons that can be given to account for this surprising fact. Apart from questions concerning the limited reliability of accident records and, indeed, of certain measures of vision, two considerations are of particular importance: First, accidents occur so rarely (in terms of total mileage) that a long, carefully checked period of exposure for a rather large group of drivers is necessary in order to obtain true measures of the tendency to have accidents. Second, accidents are so varied in the circumstances surrounding them, with so many factors contributing to their occurrence, including the sometimes critical element of chance, that *any one factor*, responsible though it may be on occasion, cannot be expected to be prominent statistically to any great extent.

That applies, no doubt, to each of several visual functions. By the same token it must be recognized that these visual functions are not all-important factors in accident causation, but they are contributing factors—like many others. Indeed, it is often difficult to consider them independently of other variables or of some broader personal function.

Medical authorities, eye specialists, physiologists, and psychologists have already provided a wealth of clinical evidence, laboratory findings, and informed opinion regarding vision, which can be used to advantage in combating accidents on our streets and highways.

VISUAL ACUITY

As far back as 1907, in the bulletin of the Society of Ophthalmology of Paris, the question was raised whether it was necessary to determine the safe minimum visual acuity of drivers. Of all the aspects of vision considered in connection with driving, acuity or keenness of vision has been the most common. As far as driver licensing has been concerned, *visual examination has usually meant no more than determination of visual acuity*—and with considerable variation among the states as to minimum standards and test procedures. It is time this misemphasis on acuity were corrected. Even the previously mentioned statistical research indicates that it is no more important than other aspects of vision, and even still significant reasons are given in the following paragraphs.

In a report by illuminating engineers from General Electric we find this significant statement:

"In most tasks of seeing, and particularly on streets and highways, contrast is a far more important factor than visual acuity, which is determined by the smallest size that can be seen or recognized. Visual

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* A very extensive investigation of the subject has been under way at North Carolina State College in cooperation with the North Carolina Department of Motor Vehicles. Results are not yet conclusive.

acuity is no measure of the visibility of most hazards to drivers and pedestrians on highways. These objects are overwhelmingly large compared with the smallest things that can be seen. They become hazards in seeing chiefly because their contrasts with their background or surroundings are too low for easy, quick, and certain seeing. Visual acuity is a criterion of value in its proper place, but it is entirely inadequate in determining visibility and ability to see outdoors on streets and highways."[28]

In an editorial of the *American Journal of Ophthalmology* in 1949 this evaluation appeared:

"Deficiencies in dark adaptation, field of vision, eye-hand and eye-foot coordination are all more significant than central visual acuity. The macular vision of accident-prone drivers does not differ from that of the average driver. Many drivers with only 20/200 vision have had no accidents in 20 years of driving. Since most hazards are very large, the perception of contrast is probably of more value than simple acuity."[22]

It is interesting to note Selling's observation in connection with the work of the Psychopathic Clinic of the Traffic Recorder's Court in Detroit. According to Dr. Selling, a man with 20/100 vision can see a car almost one-half mile away on the open road, and if he is following another car, "he can see details sufficiently at one hundred yards so that he can predict what the driver is going to do."[25]

Another general evaluation is noteworthy: At the Research Correlation Conference called by the Highway Research Board in 1952, a group of scientists studying the problem of vision came up with the report that "other factors (than visual acuity) were probably more important for highway safety."[17]

As a matter of interest, some of the minimum visual acuity standards that have been recommended are as follows:

Minimum Visual Acuity Standards for Unrestricted License to Operate a Motor Vehicle

	Better Eye	Worse Eye	Both Eyes
American Association of Motor Vehicle Administrators	(no definite standard)		
American Medical Association	20/40	20/100	———
American Optometric Association	———	———	20/40
Conrad Berens	20/40	20/200	———
J. S. Baker (National Safety Council)	20/30	20/50	———
Interstate Commerce Commission	———	———	20/40

PERIPHERAL VISION

While looking straight ahead, it is possible to see to a considerable degree on each side. This phenomenon has been termed peripheral vision, or more commonly, side vision. In the peripheral regions of the retina one cannot successfully perceive detail as in the central or foveal region of the retina. But it is an established fact that the periphery is of great value in calling attention to outlying objects, particularly insofar as gross form and movement are concerned.[11]

It would seem that peripheral vision plays an important part in safe driving. At intersections, cars approaching from the right or the left must be noticed by the driver. Between intersections, the driver must be aware of pedestrians stepping out into the road. A driver whose car is about to be passed by another must sense

that fact. In all such situations the driver generally does not have time to study the details of approaching objects. Peripheral vision, however, provides him with a helpful clue to movement on either side of his car.

It has been estimated that, normally, side vision of the right eye should extend about 90 degrees to the right side and about 60 degrees (because of interference by the ridge of the nose) to the left side; correspondingly for the left eye. This would mean a total range of 180 degrees. A number of authorities[2] feel that a field of vision of less than 140 degrees tends to make for unsafe driving.

The percentage of cases of seriously limited peripheral vision is believed to be very small. What do such restrictions signify? Serious cases are usually accompanied by other symptoms of organic or functional nervous disease; indeed they are often the result of such conditions.[11,22] Fatigue, alcoholic intoxication, certain drugs, and acute oxygen want may also cause marked contraction of the visual fields.[24] No doubt the condition is aggravated as illumination decreases.

A driver with restricted side vision would do well to drive with extra caution and at moderate speeds, particularly at dusk and during the hours of darkness. He should keep his head turned a bit toward an abnormal side, and if both sides are deficient, he may find it helpful to move his head slightly from side to side.

COLOR BLINDNESS

Red-green color blindness has been of natural concern in the field of traffic safety. But it would seem unnecessary to include a test of color blindness in driver license examinations. This conclusion is supported by a joint report of the American Optometric Association and the American Association of Motor Vehicle Administrators. There are a number of good reasons for this, apart from investigations which show practically no relation between color blindness and accidents and violations.[28]

A red-green color-blind individual may still distinguish between red and green signal lights, seeing them somewhat as a dark gray and as a light gray. This distinction is facilitated in communities where the red and green signal lights are kept in the same relative position, as has been recommended by traffic engineers for the sake of uniformity. Equally important, yellow color is usually included in the red traffic signal and blue in the green, so that discrimination is facilitated. Finally by paying closer attention to the actions of other drivers at intersections, color-blind drivers have still another means of avoiding difficulty because of their deficiency.

NIGHT VISION AND GLARE RECOVERY

These aspects of vision are believed to be of considerable importance in highway safety, even though controlled research in this area has not been very revealing (largely because of inadequate tests). It is known, for example, that the night fatal accident rate per mile of travel is three times as high as the day rate. The ratio for injuries is also believed to be significant.

Under conditions of night or low illumination, the ability to see details is strik-

ingly impaired. Davson reports that if the visual acuity in daylight is put at 100, the visual acuity in full moonlight is reduced to about 35; in half moonlight, 16; in clear starlight, 8; and under an overcast sky, only 4.

It is a somewhat redeeming feature of scotopic or night vision that objects difficult to see directly may be visible by looking to one side. This, again, is parafoveal or side vision.

Of related significance is the function of glare recovery. People differ considerably in their tolerance of and reaction to glare. Some drivers may be so blinded by glaring headlights of an oncoming vehicle that they are unable for some time to see the road ahead of them. The setting sun may have a similar effect.

To add to the problem, research has shown that night vision and glare resistance tend to diminish with age. The American Automobile Association reports that the rate of decline is slow to the age of 45 and then seems to deteriorate rapidly, particularly after the age of 65. This apparently applies as much to individuals with "normal" vision. Unfortunately, drivers generally are not aware of this loss of function, which can be compensated for only by slower and more careful driving.

Other factors may affect this function unfavorably; among them are alcohol, certain illnesses, and even .001 per cent of carbon monoxide.

Finally, studies have been made of the effect on night vision of tinted eyeglasses, tinted windshields, and filters of various kinds. There seems to be general agreement that the effect is deleterious, significantly lowering the level of visibility.[16, 21] The American Medical Association disapproves the use of these devices for night driving.

BLIND SPOTS

In a number of reports on the subject, there has been reference to "blind spots" in vision. Normally, we are not aware of the blind spot, which is a very nonreceptive part of the retina where the nerve fibres and blood vessels enter and leave, because impressions which fall on the blind spot of one side fall on a receptive area on the opposite side. This fact considerably limits any undesirable effect. It is highly debatable whether this constitutes a hazard for even a one-eyed person because the eye, even when fixed on some object, is making small rapid oscillatory movements that might bring into view whatever was obscured by the blind spot immediately before.[8]

DEPTH PERCEPTION

It is believed that in many accidents inability to estimate distance and speed is a contributing factor. This factor is obviously important to the driver in the maneuvers of passing, parking, and turning. Studies indicate that the average driver may be expected to make serious errors in judgments of speed, particularly at night when visual cues are few and not very reliable.[27] And in the process of passing other vehicles, drivers' estimates of speed and distance of oncoming cars are none too reliable.[15] It is important, therefore, to understand how these functions oper-

ate, the factors that tend to affect them, and various considerations that should be taken into account in attempting to obtain a valid measure of these functions.

There are many visual experiences on which the ability to judge distances is based. Some result from the co-ordinated activity of the two eyes; others, from impressions gained by a single eye. The binocular cues are those afforded by stereoscopic vision and convergence. Stereoscopic vision depends on the fact that when the two eyes look at the same object, each receives a slightly different image. It is commonly assumed that this factor becomes relatively unimportant beyond 60 feet or so.[8] Convergence is the movement which brings the visual axes of the two eyes to meet on an object. The degree of muscular activity required gives an indication of the position of the object. This, too, may be effective up to about 60 feet. Hence the particular significance of binocular cues in short-range activities such as parking, passing, and narrow-lane driving.

The monocular cues which can be used are numerous, interesting, and probably insufficiently recognized.

"Information may be provided by the amount of muscular activity required to change the curvature of the lens in order to bring the image of an object into focus on the retina, but this is probably ineffective as a depth cue beyond about two metres. Other possible sources of spatial discrimination are provided by the relationship of an object with other objects in the environment, such as overlapping contours or interposition, the various combinations of light and shadows, and the relative movement of one object with another or their apparent movement imposed by alterations in the position of the head and eyes (motion parallax). Indications of distance may also be obtained by apparent changes in objects as they recede from the eyes; for example, a decrease in size, brightness, contrast and detail, alterations in color, convergence of objects placed at a fixed distance apart and, if objects are moving, the reduction in their speed."[8]

Unfortunately, experimental evidence is lacking to establish clearly that the rodtype or other current tests of depth perception are valid and adequate for the purpose. For one thing, they usually depend on an estimation of the relative distance of two pegs or other objects at some more or less *fixed* distance; in actuality, the spatial relationships are commonly dynamic and changing for both objects (often more than two), and the "theatre of operation" itself may be broad and fluctuating. In reality, too, many external clues are present—a very important factor.

It may be suggested, therefore, that the best test of depth discrimination in any given situation is the situation itself. If such realistic testing cannot be done practically, the test chosen should represent as closely as possible the conditions in which the judgments of depth will actually be made. The measures obtained from the usual-type tests apply specifically to the restricted conditions of the test and can only be assumed to carry over into the real situation—an assumption that has yet to be demonstrated. *Incidentally, these observations apply perhaps as much to tests of other visual functions, e.g., side vision.*

Conditions that tend to diminish the ability to judge distance include, among other things, poor visual acuity; eyestrain; squinting; suppression of one eye; effects of tobacco, liquor, and certain drugs; fatigue; lack of oxygen resulting from improper ventilation of closed cars; poor contrast between objects and background; inadequate illumination; and fog or mist.[8]

One final, important fact: Depth perception is a learned skill; improvements can be effected by training.[19, 31]

EYE DOMINANCE AND THE ONE-EYED DRIVER

Many people tend to rely on one eye, even though the other eye may have no observable defect.[29] The reasons for such suppression are not clearly defined. Nevertheless, the implications for traffic safety are quite evident, with some research to support these implications.[26] Restricted visual fields and decreased accuracy of depth perception may well be involved.

Related knowledge is obtained when considering one-eyedness in the stricter sense; i.e., persons who have actually lost an eye or have effective vision in only one eye. Darcus has made a rather interesting report on this subject for the Medical Research Council of Great Britain. Among other things, he points out that:

"A person can achieve by active training considerable compensation for the loss of an eye. Thus, depth perception can be made more accurate by experience in using to the full available external cues and the visual fields widened by movements of the head from side to side. As this takes time, it has been proposed that a period of time should elapse before a license is granted to a person after the loss of an eye. Further compensation can be afforded by the use of an additional mirror, placed so that it brings into the field of view objects on the blind side."[8]

Various authorities have proposed that certain restrictions should be imposed in licensing of one-eyed drivers. These concern the type of vehicle, speed of operation, and hours of the day.

MUSCLE BALANCE

Each eyeball is supplied with six muscles by means of which the eye is moved freely in its bed. Normally these muscles act in concert, so that the pair of eyes is perfectly coordinated and the object being visualized appears as a clear, single object. If the muscle balance is lost there may result blurring of vision, headaches, fatigue, impairment of depth perception, and in extreme cases diplopia or double vision. Marked defects in this respect are known to be correlated with productive inefficiency in industrial occupations.[19]

Less attention has been paid to muscle imbalance as a factor in traffic safety. Esophoria—a condition in which the eyes are inclined to deviate inward—is much more common than other types of muscle imbalance and perhaps most highly associated with accident-proneness.[27]

VISUAL FATIGUE

In a number of ways driving puts a heavy strain upon the eyes: alert focusing on near and distant objects and frequent shifting of vision from near to far (for example, from instrument board to horizon) or vice versa, tend to tire the eyes.[3] Underillumination causes strain, for when an object is indistinct the eye tries to focus it better and muscular tension develops. Conversely, visual fatigue may be produced by glaring headlights and related factors. Results of visual or general fatigue may

include drowsiness, headache, a narrowing of the visual field, and impaired perception of spatial relationships.

Incidentally, fatigue and the related concept of monotony are among several factors that probably contribute to the experience of "highway hypnosis." The latter is not a separate phenomenon to be investigated alone.[17]

BLINKING AND VISUAL INTERFERENCE

In the waking hours the eyes blink quite regularly at intervals of two to ten seconds, the actual rate being more or less characteristic of the individual. The purpose of this function is to spread the lacrimal secretions over the cornea. External stimuli and the emotional state of the individual may modify his normal blinking rate.[9]

Because blinking may obviously interfere with vision, it cannot be excluded as a cause of accidents. Although this interference is of relatively short duration—up to about .5 seconds—one must consider this fact in relation to our knowledge of reaction time and stopping time on the road. Then it is clear that .5 seconds, or even somewhat less, is not insignificant for safety. This is certainly true for individuals in whom blinking has become a nervous habit, occupying a longer moment of time and likely to occur especially during periods of stress.

It is interesting to note experimental reports[25] which indicate that blinking may interfere with performance of certain tasks; and that it is frequently associated with inattention, which in itself is a cause of deterioration in performance.

ATTENTION, PERCEPTION, AND PERSONALITY

A pair of perfect eyes is in itself no guarantee of freedom from accident, not even if their possessor is in generally good health. To help ensure against accidents, one's visual apparatus must be properly used. Does the individual attend to the scene while driving? How ready is he to respond? What does he actually *perceive* in relation to what he is *able* to see?

It is not within our province here to consider the implications of these questions in detail. The concepts of attention, perception, and personality are intricate and interrelated. However, some fact and theory may be mentioned briefly to underscore the significance of the problem.

(1) It seems probable that more continuous attention from moment to moment is required of the motor vehicle driver than of the operator in any other type of transportation, including the airplane.[17] In this connection, one state (Pennsylvania) reports that "inattention" appears to be by far the greatest single cause of fatal accidents, so far as condition of the operator is concerned.

(2) The driver must both distribute and concentrate his attention according to the immediate need. He must attend to many things in the traffic scene, focus on particular aspects as required, yet not divert so much attention in one area that he fails to take precautions in another.[4]

(3) A driver is able to see an unexpected obstacle only about half as far away as he can see an expected one.[37] This is a particularly significant research finding, which highlights the need for *anticipatory* driving.

(4) There are numerous factors that may cause relaxation of attention. These range from momentary distraction by car radio or car conversation to the more significant effects of emotional preoccupation and highly routinized behavior. For example, the latter is illustrated by implication in a study by the Baltimore and Ohio Railroad. This study disclosed that in more than 90 per cent of a group of grade-crossing

accidents, the automobiles involved bore local registrations and were driven by persons living nearby—and therefore familiar with the crossings!

(5) It is impossible, in practice, to separate the sensation of seeing, the act of attending, and the perceptual process. The visual sensation is "integrated" with sensations from other sources, and more important still, with the memory or effects of past experience. The result is the interpretive process known as perception. It is a selective process depending upon the task to be performed.

For another example, when you are driving your car, and there looms before you another vehicle which you decide to pass, what actually do you perceive in this situation? The make of the car? Its color? Its approximate age? Hardly. To you it is an object to be passed. The details of the situation that you actually *see*—in other words, that you *perceive*—are those that are meaningful for the purpose of passing. Visual acuity is a small factor here: one is not concerned with fine details of the car. What you probably do perceive with more or less accuracy is the approximate speed with which the vehicle is moving; its position on the road in terms of a clearance space; and similar factors with regard to other vehicles that may be approaching in the opposite direction. You interpret these as intentions of other drivers in relation to what you want to do.

(6) It has been hypothesized and demonstrated in a way that individuals with low perceptual speed relative to their speed of response would be particularly likely to have accidents, responding before they had adequately perceived the situation.[10] In other words: slow to "see" . . . quick to respond . . . the likely result—a wrong response. Further studies along this line are warranted.

(7) Nothing can interfere more with the function of attending and perceiving than a condition of preoccupation. To be preoccupied (consciously or unconsciously) means that we are "living in another world than that of perception. We cannot drive completely adequately in the traffic world and at the same time be occupied inside ourselves with emotional complexes."[28]

(8) The foregoing is particularly characteristic of persons with underlying problems of personality and adjustment. There is an increasing body of literature to indicate that these problems constitute the primary cause of so-called accident proneness, whereas no important differences between accident repeaters and accident-free drivers have been found with respect to visual functions and other psychophysical traits. The two groups are being differentiated in terms of impulsiveness, aggressiveness, lack of responsibility, and related symptoms of maladjustment.[12, 33, 38]

(9) The attention and perception of even so-called normal people are unfavorably affected under certain circumstances that may occur day in and day out. Fear, worry, temporary stress and strain, all tend to make any one of us accident prone, at least temporarily. The visual functions as such are not impaired. But we are obviously less alert to environmental hazards; we do not perceive a hazardous situation as we ordinarily would; normally desirable attitudes toward safe driving just do not seem to come into play. This is extremely important, because most accidents happen to "average drivers" rather than to accident repeaters. And it seems safe to say that these average drivers are for the most part persons with normal vision. This is a topic that could be pursued at great length. Suffice at this time to raise the questions: Why test the vision of people simply under conditions of rest? What happens to this vision under emotional stress or in driving emergencies? This is a real, dynamic aspect of the problem.

EXTERNAL FACTORS AFFECTING VISUAL FUNCTIONS

It is beyond the realm of this paper to consider even briefly the external factors that affect visibility from a driver's seat. Obviously, smoke, fog, haze, smaze, and smog make poor vision poorer. Inadequate illumination on streets and highways makes seeing more difficult. Vicissitudes of weather and terrain are well known for interference with vision. Finally, there are the special problems created by ineffective location of traffic signs, questions of legibility of sign copy, and matters of color scheme, size, and shape of signs. A great deal of information-producing research has been done in these areas and much of it has been fruitful.[14, 30] We would be remiss not to acknowledge the existence of these other related areas of research and the many accomplishments therein.

POSSIBLE SOLUTIONS

Up to this point the author has been considering a lengthy series of medical, physiologic, and psychologic facts and opinions concerning vision and driving. Yet by no means has this been a comprehensive list. Conditions like astigmatism, aniseikonia, and numerous others are also pertinent to the subject. And the sum total of available evidence suggests that no one visual factor is prominent far beyond the others in accident causation; certainly it is not possible to completely dismiss any one of the factors mentioned. What then can be done with the known facts and their implications in order to improve street and highway safety?

Driver Licensing. Obviously, it is utterly impractical to take into account in driver licensing, individually, all the visual factors considered pertinent. The licensing problem is a huge one; some six million drivers are examined annually. Yet at the present time it is clearly the merest token of an examination when only visual acuity and occasionally one or two other factors are checked, and because of limitations in time, budget, and manpower, checked very crudely.*

It is fundamental to consider these facts: first, that there are many possible types of visual defect; second, that a high rating in one visual function does not preclude a poor rating in another; third, that visual problems may contribute to behavioral problems; and fourth, that the eye, as an integral part of the body system, "may become involved or affected in the course of almost any disease."[32] The latter possibility runs the gamut from infectious diseases and glandular disorders to diseases of the cardiovascular system and nervous and emotional disorders. Millions of our adult population are concerned at any given moment, even from a chronic point of view.

For licensing purposes, therefore, it seems reasonable to suggest the following:

(1) A general medical examination (by a physician of one's own choice) such as is now required by the Interstate Commerce Commission in the case of interstate operators, for the detection of gross conditions that may impair driving performance through disturbance of vision or other functions;

(2) As part of this examination, a screening of visual acuity. In view of the considerable difference of opinion as to what constitutes a suitable standard, it is suggested that the American Medical Association's recommendation of 20/40 in the better eye and 20/100 in the poorer eye be adopted for screening (rather than rejection) of license applicants. Failure to meet this standard would then mean referral to a vision specialist of one's own choice for evaluation of the condition. His recommendation would be reviewed by the licensing authority, which, of course, would make the actual determination with regard to rejection of application or granting of a regular or restricted license. (This screening procedure, in principle, has been viewed favorably by the American Association of Motor Vehicle Administrators and the American Optometric Association.)

(3) Periodic re-examination along the lines suggested above. (Medical re-examination every three years is already required by the I.C.C.) Bodily conditions change with age, and this is certainly true of visual skills. Visual efficiency drops with advancing years, particularly (according to several studies) in the late fifties and thereafter. Apart from the effects of age, vision may for many reasons deteriorate from a level that was acceptable at the time of original licensing. Furthermore, it is possible for the indi-

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* It should be noted, however, that several states are now using newer types of visual examining equipment that not only avoid some of the problems encountered in testing visual acuity by means of the Snellen Chart but also provide measures of other visual functions.

vidual to be ignorant of the change and therefore fail to adjust his driving accordingly. Correction and re-education are important needs here.

As a corollary to this licensing program it is suggested that in the case of acute and chronic illnesses, physicians advise their patients of any conditions that may endanger their safety on the road. This advice might well cover drugs and chemicals used in treating these illnesses, if they may have intoxicating effects that can disturb vision.

Subjects for Further Research. It is apparent from the discussion of driver licensing, and particularly from the textual matter preceding this discussion, that there is a great need for further research on various aspects of vision in motor vehicle operation. This is not to detract from the many valuable contributions that have already been made by the various disciplines. However, there is sufficient reason at this point to mention some of the more important research needs.

(1) There is a general need for translation and application of laboratory data to the highway situation.

(2) Tests of certain functions, particularly of depth perception and peripheral vision, need to be made more realistic, to conform as much as possible to the actual and dynamic circumstances of motor vehicle operation.

(3) More valid and reliable tests for night vision and glare resistance are very much needed.

(4) It seems highly desirable to conduct studies testing visual acuity and other visual functions under conditions of emotional stress or preoccupation, for comparison with visual performance under conditions of rest. The former conditions often prevail in actual driving; the latter, however, have generally obtained in driver licensing and vision research concerned with traffic safety.

(5) In studies comparing accident repeaters and accident-free drivers, it would seem desirable to take into account the visual abilities of the two groups at the approximate time of occurrence of accidents, before generalizations are made regarding differences in visual abilities as factors in accident causation.

There are, of course, still other research needs. The foregoing simply identifies some of the more immediate problems that need to be solved. To this list, however, must be added an area for research which holds unusual promise. This has to do with the relatively new field of visual training.

Visual Training. In addition to lenses, visual correction may be effected by training. This newer form of correction has been given the name "orthoptics." Essentially, it is a system of graded, repetitive exercises for the eyes, with and without special instrumentation.[11, 20] So far, orthoptics has been used principally in the treatment of strabismus or squint—and in any case, primarily with children. But it has much broader values and applications, at least potentially, in the stimulation and development of vision.* Not only may faulty visual habits be corrected; indeed, some visual skills that we now consider normal or average may be brought to a significantly higher level of accomplishment. In a way this possibility was dramatically illustrated in tachistoscopic training in airplane recognition during the second World War. Through this method Renshaw found that ordinary people could rapidly achieve a degree of skill previously considered of the order of genius:

* This view was recently emphasized by Dr. Conrad Berens, Chairman of the National Research Council's Armed Forces Vision Committee, in a private discussion with the writer.

they learned to see and identify features of objects or forms when the "flash" presentations were reduced to a very small fraction of a second. Industrial experiments are yielding supporting evidence. Orthoptics in the broader sense offers many other possibilities.

Insofar as traffic safety is concerned, if through such visual training of present and future drivers we can effect improvement and advanced development in speed, scope, and precision of certain visual functions, with reduction in fatigability of function, it may well result in a very important contribution toward the solution of a serious national problem. Experimentation with visual training in conjunction with driver education is definitely warranted.

In this connection, it seems necessary to point out that, despite certain interpretations of the findings of a number of psychologic studies, it is only the *rare* individual who, knowingly or otherwise, seeks to destroy himself. Given certain skills—including various *visual* skills—the average person will consciously or unconsciously use them to anticipate or outmaneuver any threat to his person or property. And if he has these skills to a sufficient degree, he may be expected to do so with success. This applies not only to driver but also to pedestrian—not only in traffic but on the job and in most other areas of human activity. And given desirable attitudes, through proper education, the individual may also be expected to use his advanced skills not only for his own safety, but also for the protection of others. This, of course, is the ultimate objective of all safety programs.

BIBLIOGRAPHY

1. American Association of Motor Vehicle Administrators and the American Optometric Association: Manual on Driver's Vision Test. Pittsburgh: American Optometric Association, 1949.
2. Baker, J. S.: Drivers' License Eye Test Standards (Public Safety Memo. 42), Chicago, National Safety Council, 1938.
3. Berens, Conrad: Certain eye factors in the prevention of motor vehicle accidents, New York State J. Med. *40*:1713 (Dec. 1, 1940).
4. Brakeman, E. E., and Slocombe, C. S.: Review of recent experimental results relevant to the study of individual accident susceptibility, Psychological Bulletin. *26*:15 (January) 1939.
5. Bransford, T.: Relation of Performance on Driver's Tests to Automobile Accidents and Violations of Traffic Regulations in the District of Columbia, Unpublished Doctor's Dissertation, American University, Washington, D. C., 1939.
6. Brody, L.: Personal Factors in Safe Operation of Motor Vehicles. Center for Safety Education, New York University, New York, 1941.
7. Cobb, P. W.: Automobile Driver Tests Administered to 3663 Persons in Connecticut, 1936–37, and the Relation of the Test Scores to the Accidents Sustained. Unpubl. report to Highw. Res. Bd., Washington, D. C., July, 1939.
8. Darcus, H. D.: The One-Eyed Driver, Oxford, Medical Research Council for Research on Climate and Working Efficiency, 1952.
9. Davson, Hugh: The Physiology of the Eye, Philadelphia, Blakiston, 1949.
10. Drake, C. A.: Accident-proneness: a hypothesis, Character and Personality. *8*:335 (No. 8) 1940.
11. Duke-Elder, Sir W. S.: Textbook of Ophthalmology, Vol. IV, The Neurology of Vision, Motor and Optical Anomalies, St. Louis, C. V. Mosby, 1949.
12. Dunbar, F.: Emotions and bodily changes: A report of some recent psychosomatic studies, Ann. Int. Med. 837 (No. 14) 1940.
13. Eno Foundation for Highway Traffic Control: The Motor-Vehicle Driver: His Nature and Improve-

ment, Saugatuck, Connecticut, The Foundation 1949. 165 pp. (Obtainable from the Center for Safety Education, New York University).
14. Forbes, T. W.: Street and Highway Traffic, in Handbook of Applied Psychology, New York, Rinehart, 1950, vol. I.
15. Forbes, T. W., and Matson, T. W.: Driver Judgments in Passing on the Highway, J. of Psychol. *8*:3, 1939.
16. Highway Research Board: Effect of Tinted Windshields and Vehicle Headlighting on Night Visibility, Highway Research Board Bulletin No. 68, Academy-Council Publication No. 259, 1953, 66p.
17. Highway Research Board: Report of Highway Safety Research Correlation Conference, Washington, D. C., Committee on Highway Safety Research, 1952.
18. Interstate Commerce Commission: Motor Carrier Safety Regulations. Washington, D. C., Government Printing Office, 1952.
19. Kuhn, H. S.: Industrial Ophthalmology, St. Louis, C. V. Mosby, 1944.
20. Lancaster, J. E.: A Manual of Orthoptics, Springfield, Ill., Charles C Thomas, 1951.
21. Lauer, A. R., and Stone, J. A.: The effect of certain wave-length contrasts on discrimination thresholds under mesopic vision, Unpublished paper presented at the annual meeting of the Highway Research Board, 1954.
22. Lebensohn, J. E.: The motor vehicle driver, Am. J. Ophth. 32:592 (April) 1949.
23. Luckiesh, Matthew, and Moss, Frank K.: Quick and Certain Seeing on Streets and Highways, in Seeing and Traffic Safety, Cleveland, General Electric Company, 1940. Part I, p. 6.
24. McFarland, R. A.: Human Factors in Air Transportation, New York, McGraw Hill, 1953.
25. Poulton, E. C., and Gregory, R. L.: Blinking during Visual Tracking, Cambridge, Medical Research Council, Applied Psychology Research Unit, 1951.
26. Quinan, C.: The handedness and eyedness of speeders and of reckless drivers, Arch. Neurol. & Psychiat. 25:829 (April) 1931.
27. Roper, V. J., and Howard, E. A.: Seeing with motor car headlamps, Transactions of the Illuminating Engineering Society, 1938, p. 417.
28. Selling, Lowell S.: Abnormalities of the eye and their significance in traffic court cases, J. A. M. A. *113*:994 (Sept. 9) 1939.
29. Selzer, Charles A.: Lateral Dominance and Visual Fusion (Harvard Monographs in Education No. 12) Cambridge, Harvard University Press, 1933, 119pp.
30. Smeed, R. J.: Some factors affecting visibility from a driver's seat and their effect on road safety, Brit. J. Physiol. Optics. *10*:63 (June) 1953.
31. Snell, A. C.: The need for a more realistic ophthalmic service in industry, New York State J. Med. *42*:1435, 1942.
32. Tassman, I. S.: The Eye Manifestations of Internal Disease, St. Louis, C. V. Mosby, 1942, 542 pp.
33. Tillmann, W. A., and Hobbs, G. E.: The accident-prone automobile driver, Am. J. Psychiat. *106*:321, 1949.
34. Traffic Engineering and Safety Department, American Automobile Association: Age and the Ability to See at Night, Research Report No. 43, Washington, D. C., The Association, 1953.
35. Van Lennep, D. J.: Psychological factors in driving, Traffic Quarterly. *6*:483 (October) 1952.
36. Visual Standards for Licensure to Operate Motor Vehicles: Preliminary Report of Special Committee, J. A. M. A. *109*:61B (Oct. 16) 1937.
37. Weiss, Albert P., and Lauer, Alvah R.: Psychological Principles in Automotive Driving, Contributions in Psychology, No. 11, Columbus, Ohio State University, 1939, 165 pp.
38. Wisely, Harold Martin: Personal Characteristics of Commercial Bus Drivers Related to Accident Proneness, Ph.D. Dissertation, Evanston, Illinois, Northwestern University, 1947.
39. United States Air Force School of Aviation Medicine: The Human Factor in Accidents with Special Reference to Aircraft Accidents, Randolph Field, Texas, The School, 1951.

ABSTRACTS

OPTICS, PHYSIOLOGY, AND PSYCHOLOGY OF VISION

27. *Color and Vision.* HARRY HELSON, Austin, Texas. Illuminating Engineering. *49*:92–93, February 1954.

The visual mechanism, so far as light and color are concerned, averages energies impinging upon the eye according to their distribution in space and time. Within a given viewing situation a zero point of function is established which is a weighted log mean of all stimuli in the field of vision. Through shifting its zero point or adaptation level, the eye can function over a range of energies amounting to 50 billion to 1. But for any given adaptation level the actual range is limited to about 100 to 1.

Various methods of determining the colors of objects in widely different sources of illumination show that objects above adaptation reflectance are tinged with the hue of the illuminant, and objects below adaptation reflectance are tinged with the hue complementary to the hue of the illuminant. This principle helps explain changes in colors of objects in passing from daylight to artificial sources of illumination. Since colors of objects are determined largely by the differential between object and background reflectances, changes in background may influence object colors more than considerable change in spectral energy distribution of the illuminant. 1 reference.—*Author's abstract.*

28. *Some Neural Correlates of Visual Experience.* FRANK RAY WILKINSON. Am. J. Optom. & Arch. Am. Acad. Optom. *31*:122–126, March 1954.

There are few known relationships between physiologic processes in the optic pathway and cortex and perceptual events. Among the few are the following: (a) the two-flash phenomenon in which the perceptual event of two distinct flashes was shown by Bartley and Wilkinson to correspond in latency and necessary stimulus conditions to an unexplained second wave in recordings of nervous activity in the optic nerve, and (b) brightness enhancement in which a maximum reversal of Talbot's law was found by Bartley at a stimulus pulsation frequency which coincides with cortical alpha rhythm and in which the fluctuation of entoptic stray light was found by Bartley and Wilkinson to be an important factor. A third possible relation may exist between hypothecated perceptual events and the process of organizing the parallel circuits in the optic pathway which intermittent stimulation at certain frequencies seems to accomplish. Research is now in progress on this problem. These examples lead us to hope that perception may eventually be described in terms of the neural events involved. 7 references.—*Author's abstract.*

PHYSIOLOGY, CHEMISTRY, AND BIOCHEMISTRY OF THE EYE

29. *The Electrical Responses of the Eyes; Part III—The Electroretinogram.* DAVID D. MICHAELS. Am. J. Optom. & Arch. Am. Acad. Optom. *30*:588–596, November 1953.

This is the third in a series of papers dealing with the electrical responses of the eye. A historical review of electroretinogram analyses is followed by a discussion of its general theoretical and clinical significance. The electroretinogram obtained from simple eyes is contrasted to the responses of more complex retinas. Methods of isolating the individual components of the curve are evaluated and their source of origin is considered. It is concluded that at the present time the ERG can be most reasonably incorporated into a frame of reference derived from a somewhat extended duplicity theory. A brief summary of the relevant instrumentation and of some recent clinical application to human eyes is presented.

30. *The Electrical Responses of the Eye; Part IV—Some Sensory and Clinical Applications.* DAVID D. MICHAELS. Am. J. Optom. & Arch. Am. Acad. Optom. *30*:644–654, December 1953.

This concluding paper in a series dealing with the electrical responses of the eye draws a few selected comparisons between sensory and neurophysiologic data. Visual adaptation, discrimination, and the duplicity theory are considered. 134 references.—*Author's abstract.*

PATHOLOGY, BACTERIOLOGY, AND IMMUNOLOGY

31. *The Histological Interpretation of Fundus Lesions.* O. B. RICHARDSON. Tr. Canad. Ophth. Soc. *6*:70, 1953.

Recently the round hemorrhages seen in diabetes have attracted attention. Ballantyne and Loewenstein have discovered that many of these red spots are capillary aneurysms. They are uniform in size—50 to 60 microns in diameter. Most are found in the inner nuclear layer, although they are occasionally present in the ganglion cell or the nerve fibre layer. They may rupture and produce a true hemorrhage. Swelling and proliferation of the endothelium, thrombosis in the aneurysm, may lead to a scarred nodule. The walls of the retinal capillaries may show a hyaline thickening similar to that found in the renal glomeruli of patients with diabetes.

Cotton wool patches are often an outstanding feature of albuminuric retinitis. These, histologically, are collections of globular bodies in the nerve fibre layer. These may be swollen nerve fibres, giant neuroglial fibres, degenerating glial cells, or may represent infarcts.

Senile macular degeneration appears as a fine pigmentary change, with rings and dots surrounding a pale fovea. Pathologically it is seen as sclerosis of the choroidal vessels with patchy involvement of the choriocapillaris. There is clump-

ing and loss of pigment in the retinal pigment epithelium in some areas and proliferation of epithelium in others.

A disciform degeneration of the macula in its early stages appears as a grey mound; later it becomes white in color and is frequently covered with blotches of pigment. Histologically, proliferation of the pigment epithelium forms a prominent component of the mound. The retina over the mass is atrophic and disorganized. Proliferating pigment epithelial cells, fibrous tissue, blood, and albuminous exudates may all be present in the mound. It is suggested that this condition starts as a hemorrhage which bursts through Bruch's membrane and lifts up the retina. The proliferation of pigment epithelium follows and with organization of the mass of blood causes a mound.—*Clement McCulloch, M.D.*

32. *Chronic Progressive External Ophthalmoplegia; A Clinical and Neuropathologic Report.* GABRIEL A. SCHWARZ AND CHAN-NAO LIU. Arch. Neur. & Psych. *71*, January 1954.

The authors' patient, a white male, died at the age of 63 years from a spongioblastoma polare of the left parietal lobe. At the age of 27, he had begun to have drooping of his left upper eyelid. At 41 years of age ptosis began on the right side. The onset of weakness of the movements of his eyeballs had come so insidiously that no definite time of onset could be established. When examined the year before his death the patient showed bilateral ptosis, the eyeballs in primary position, only barely perceptible movements of his eyeballs either voluntarily or reflexly, pupils which were equal and regular and round and reacted well to light but poorly to attempted convergence. The other cranial nerves were intact.

Neuropathologic studies of the oculomotor, trochlear, and abducens nuclei showed the cellular populations to be unchanged, the motor neurones to be somewhat smaller, less polygonal and rounder than usual, and cytoplasmic clumps of granular yellow-brown pigment and a few vacuoles in some perikarya. The intra-axial and extra-axial portions of the oculomotor, trochlear, and abducens nerves showed no demyelinization.

The left superior oblique, the left superior rectus, and the right lateral rectus muscles were found to show a marked and diffuse destruction and loss of muscle fibers. The remaining muscle fibers showed many changes. Large and small fibers were seen. Myofibrils in some were swollen and torn apart. Portions of muscles were hyalinized. Areas of muscles were granular. A few fibers looked fairly normal. Even in one single muscle fiber there were these varied alterations. There was a marked increase in the sarcolemmal nuclei about the muscle fibers. Fat and connective tissue replacement and overgrowth occupied much of the muscles. The myelin stain and the axis-cylinder stain disclosed abundant intact intramuscular nerve fibers. Motor end-plates could be identified on severely degenerated muscle fibers or apparently free in the loose connective tissue.

In the authors' case the changes in the extraocular muscles were felt to be typical of changes described late in muscular dystrophy. In the affected muscles there was preservation of abundant nerve fibers and the presence of motor nerve endings.

These findings, coupled with the preservation of the intra-axial and extra-axial nerve fibers supplying the diseased muscles and the relatively healthy motor nerve cell bodies of the nuclei which gave rise to the motor nerves to the abnormal muscles —all of these findings considered together seem to us to favor the opinion that chronic progressive external ophthalmoplegia is a form of muscular dystrophy and could rightfully be called "ocular myopathy."

DIAGNOSTIC METHODS OF EXAMINATION, BIOMICROSCOPY AND PHOTOGRAPHY

33. *The Cover Test in Clinical Practice.* PHILIP G. SLOAN. Am. J. Optom. & Arch. Am. Acad. Optom. *31*:3–11, January 1954.

The cover test is one of the oldest tests of ocular motility. In this field, it occupies a position comparable to that held by retinoscopy in the estimation of refractive error. The cover test permits a complete elimination of fusional stimuli and more truly establishes the "fusion-free position" sought in heterophoria testing than do the distortion or dissociation tests. As an objective test, it may be used when subjective testing would be suspect. Accuracy in measurement is limited by the examiner's experience and skill in detecting small movements of the eyes, rather than the judgment of the patient.

The procedures for the detection, classification, and measurement of heterophoria and heterotropia are described, as well as possible errors in technic. Attention is drawn to such modifications of the cover test as the screen Maddox-rod and parallax tests.—*Author's abstract.*

ANOMALIES OF REFRACTION AND ACCOMMODATIONS, CONTACT LENSES

34. *Balancing Accommodation and Convergence by Decentration of Lenses.* C. H. ANDREWS. Tr. Canad. Ophth. Soc. *6*:151, 1953.

Less than 10 per cent of lenses should be centred to coincide with the pupillary distance. Discomfort, produced by glasses, is more often brought about by their use for near vision. Glasses, therefore, should be centred for near vision. If the lenses are centred for near vision the hypermetrope will be relieved of some convergence.

Decision as to the position of the ocular centres of the lenses can be decided when data are secured as to whether or not accommodation and convergence are ample for the age, and what reserve of convergence is available. This can be obtained from an ampliometer. When the slide is set at the patient's age, he should be able to read the chart with ease. If he can the accommodation is ample. A six diopter prism is placed in the trial frame, prism base up, before one eye. If the two dots on the ampliometer appear directly above one another convergence

is ample. The slide is then moved towards the nose until the black line on the card doubles and the two red dots are not directly above one another. This distance then indicates the reserve convergence at reading distance. With these data one is reasonably decided whether to reduce the plus strength and bring more accommodation-convergence into play or whether to help convergence by prism base in.

The old-fashioned cycloplegic and postcycloplegic test is rapidly becoming an anachronism. This is time consuming and expensive to the out-of-town patient. A more rational approach would be to do a manifest refraction and then with the trial frame in place survey the accommodation and the convergence. The cycloplegic test would be merely a confirmation of the refraction proper. With all this data a prescription could be issued with the accommodation and the convergence balanced.

Prism not representing more than two millimeters of decentration can be ordered as lens decentration. If the prism is greater than that, it should be prescribed as prism. 7 references.—*Clement McCulloch, M.D*

35. *An Investigation of Visual Performance Among Selected Groups of School Children.* NEWELL C. KEPHART AND ROBERT M. UNGER. Am. J. Optom. & Arch. Am. Acad. Optom. *30*:635–643, December 1953.

Retinoscopic examinations were administered in the spring and autumn to children in grades four through eight in two schools representing rural and urban populations. The technic of analysis of variance was used to evaluate the data.

The visual status differed between rural and urban children, the urban children being more myopic. A change in visual performance occurred during the summer period, a lesser degree of myopia being evident in the fall. Though uncertain, a possible difference may exist between right and left eyes, the left eye being more myopic.—*Author's abstract.*

36. *Contact Lenses: Some Aspects of Visual Acuity and Photophobia.* JAY M. ENOCH AND JAMES L. MC GRAW. Am. J. Optom. & Arch. Am. Acad. Optom. *31*:12–28, January 1954.

Corneal clouding, resulting from contact lens wear causes diffraction, filtering, and scattering of light. Consequently, one might expect lowered acuity, especially in the presence of varied illumination. Photophobia has long been known to plague the contact lens wearer.

Instrumentation was constructed which afforded control of both target and ambient illumination. Ten subjects, fitted with four representative types of contact lenses and spectacles, were employed in these and in other extensive tests of contact lens performance.

After development of corneal clouding the fluid lens wearers showed a marked drop in visual acuity in the presence of surround illumination. Further reduction was noted on lens removal; however, vision returned to normal in one-half hour.

There was essentially no change in acuity with either spectacles or the ventilated and corneal types of contact lenses (which generally do not cause corneal haze). Many subjects could not tolerate the corneal lenses, and their acuity decreased in the presence of pain and photophobia.

Extreme variations in temperature resulted in changes in both visual acuity and photophobia, while low pressure, as tested, did not.

There are apparently two types of photophobia experienced by the contact lens wearer, one caused by ocular irritants, and another caused by veiling glare, from light scattered by the cornea. The wearers of ventilated contact lenses and spectacles did not generally manifest this problem.—*Author's abstract.*

CRYSTALLINE LENS

37. *Suction Cup for Cataract Extraction and Insertion of Ridley's Lens.* LOPEZ SILVAN. Arch. Soc. oftal. hispano-am. *13*:672–681, June 1953.

This is a preliminary report on the construction of a suction cup made entirely of rubber. Silvan designed it to increase suction power. A cup made entirely of rubber exerts a suction provided by the vacuum and by capillarity. He describes the various models he designed in search for a perfect model. The result is a cup which is applicable to cataract extraction, and which facilitates the introduction of the Ridley lens. 4 figures.

38. *Pseudo-Exfoliation of Lens Capsule.* GEORGIANA DVORAK THEOBALD. Am. J. Ophth. *37*, January 1954.

The previously undifferentiated "exfoliation of the lens capsule" is separated into two clinically and pathologically distinct entities. A condition closely resembling true capsular exfoliation of the lens is shown to be pseudo-capsular exfoliation. Pathologic descriptions of three cases of "pseudo-capsular exfoliation" are presented.

True capsular exfoliation is most often seen in glass blowers and persons exposed to extreme heat for long periods of time. It is characterized by an actual rupture of the thin transparent anterior layers of the lens capsule which become shredded or curled into a scroll.

Pseudo-capsular exfoliation has no occupational relationship. It is characterized by the deposition of an unknown substance on the anterior lens surface giving it a frostlike appearance and on the ciliary processes and zonules like iron shavings attracted to a magnet. The substance also fills the trabecular spaces and canal of schlemm and is phagocytized by the cells of the iris and cornea.

Glaucoma frequently results from pseudo-capsular exfoliation, while cataracts are more commonly associated with true capsular exfoliation.

Further study is necessary to reveal the nature and source of this material which is so often mistaken for true exfoliation of the lens capsule.—*Harold O. Kirk, M.D.*

UVEAL TRACT AND SYMPATHETIC OPHTHALMITIS

39. *Uveitis in Children.* SAMUEL J. KIMURA, MICHAEL J. HOGAN, AND PHILLIPS THYGESON, San Francisco, Calif. Arch. Ophth. *51*:80–88, January 1954.

Forty-seven cases of uveitis in patients under 16 years of age were studied during the course of surveying uveitis cases at the Francis I. Proctor Foundation for Research in Ophthalmology, University of California Medical Center. There were 18 cases of anterior uveitis and 29 cases of posterior uveitis. No cases of generalized or diffuse uveitis were noted. An etiologic diagnosis, definite or presumptive, or a specific disease association, was determined in 6 of the 18 cases of anterior uveitis. Of the 29 cases of posterior uveitis only a presumptive diagnosis of toxoplasmosis (10 cases) could be made. The practical importance of determining the presence or absence of congenital toxoplasmosis is emphasized. In spite of the reported high incidence of tuberculous uveitis in children, especially in the European literature, the authors were unable to make even a presumptive diagnosis in their series. The various causes of uveitis in children are reviewed briefly along with the differential diagnosis. It was evident from this study that posterior uveitis is common in children but anterior uveitis is rather rare. 27 references. 8 tables.—*Author's abstract.*

40. *Harada's Disease—Vogt-Koyanagi Syndrome: Diffuse Melanitis.* H. E. CRAWFORD, Hilo, Hawaii. Hawaii M. J. *13*:26, September-October 1953.

This article reports 2 cases of a rare entity which seriously affects the eyes. The disease is characterized by bilateral uveitis with retinal detachment, with development of one or all of the following conditions: headache, meningismus, deafness, dizziness, poliosis, virtiligo, and alopecia. The distinction between Harada's disease and Vogt-Koyanagi syndrome depends on the location of the ocular inflammation; in Harada's disease it is limited to the posterior segment, carrying a somewhat better prognosis; in Vogt-Koyanagi syndrome the iris and ciliary body are involved. Loss of vision is rapid, progressive, and usually complete in two weeks. Dizziness and deafness appear about the second week, virtiligo, poliosis and alopecia appear later. The prognosis is always grave and there is no treatment of demonstrated value. The second case presented is unusual in that tissue removed by iridectomy showed microscopic changes similar to those of sympathetic ophthalmia and treatment with cortisone produced a remission but the disease reappeared when it was discontinued. Its use should be continued to achieve a cure. It appears that the disease involves the pigment or melanin bearing tissues. There is melanin in the uveal tract, and the disease is most intense in the eye. There is melanin in the skin and in the hair. This accounts for the vitiligo and poliosis, and presumably the disturbance of the pigment in the germinal layer of the hair follicle accounts for the loss of hair. A disturbance in the pigment granules in the cells of Hansen in the organ of Corti could explain the deafness, and involvement of the pigment granules in the hair cells of the utricle, saccule, and ampullae of the semicircular canals can account for the dizziness that

sometimes occurs. Melanoblasts are found in the pia mater of the ventral surface of the medulla oblongata. The presence of meningismus with an increased cell count in the spinal fluid could be the result of involvement of this tissue. The essential factor of Harada's disease and of the Vogt-Koyanagi syndrome seems to be an inflammation of the melanin bearing tissues, either on an allergic or an infectious basis. The author feels that the term "diffuse melanitis" is preferable to the eponymic designations.

EYELIDS

41. *Treatment of Chronic Lid Conditions.* A. A. SINISCAL, Rolla, Missouri. Eye, Ear, Nose & Throat Monthly. *33*:221–228, April 1954.

Chronic lid conditions appearing commonly in practice are presented with a discussion of differential diagnostic points and the modern method of treatment. Conditions included are trachoma, follicular conjunctivitis, vernal catarrh, inclusion blenorrhea, blepharitis marginalis, trichiasis and districhiasis, symblepharon, ankyloblepharon and blepharophimosis, entropion, ectropion, lagophthalmos, Parinaud's conjunctivitis, and oculoglandular tularemia. Trachoma remains a disease of importance clinically because of the late sequelae and lid deformities resulting from many decades of slow cicatrization. Ocular tularemia is not as rare an occurrence as is generally supposed, particularly in suburban and rural areas where household pets may have contact with infected rodents. The routine exposure of the upper eyelid and retrotarsal fold is illustrated with 3 figures, and the operative procedure for entropion is illustrated with 8 figures.

42. *Comments on the Use of the Ptosis Crutch.* ARTHUR E. TILLISCH. Am. J. Optom. & Arch. Am. Acad. Optom. *31*:137–139, March 1954.

The ptosis crutch should be designed to provide not only a firm support for the eyelid, but to render a gentle massaging action to the eyeball. This, the author hypothesizes, aids the ocular muscles to regain tonicity and may have a beneficial action on the nerves involved.

Along with this device, excess plus is recommended initially as lessening the strain on accommodation, permitting vision to be exercised at near on small and easily integrated contours and providing some magnification effect. Maximum tint is also desirable initially if both eyelids have been normally depressed. Both plus and tint are gradually reduced.

For unilateral ptosis, when the patient has achieved a mode of uniocular vision which it may not be desirable to disturb, the ptosis crutch can still have cosmetic value, since it may be rendered nearly invisible when skillfully constructed.

A case history is provided of bilateral ptosis. Visual acuity was brought from 20/400 to 20/20 O.U. by the above procedures.—*Author's abstract.*

43. *Surgical Correction of Spastic Senile Entropion: A New Method.* DANIEL B. KIRBY. Am. J. Ophth. *36*:1372, October 1953.

Doctor Kirby maintains that the basis of the development of spastic senile entropion was due to senile degenerative flaccidity and elongation of the lower eyelid, and that the spasticity of the orbicularis muscle may be simply coincidental at the particular time that the entropion develops. He discusses various procedures which had been used, traction by tape, sutures, clamps, the production of cicatrices, resection of skin and orbicularis and transplantation of the tissues, most of which create traction on the eyelid margin.

A new procedure for the correction of spastic senile entropion described by Dr. Kirby consists in the resection of the dense tissues of the lower eyelid and their advancement temporally over the canthal ligament and lateral orbital margin, thereby shortening and tensing the lower eyelid. This procedure has been successful in the hands of the author, correcting the flaccidity and elongation of the degenerated eyelid tissues of the elderly or senile group of patients.

The technic may also be indicated in cases of flaccidity and elongation of the lower eyelid due to persistent seventh cranial nerve paralysis.—*Conrad Berens, M.D.*

RETINA

44. *Angiomatosis Retinae (Von Hippel's Disease) 11 Years After Irradiation.* FREDERICK C. CORDES AND ARIAH SCHWARTZ, San Francisco, Calif. Am. J. Ophth. *36*:1362–1367, October 1953.

Angiomatosis retinae occurs most commonly in young adults at an average age of 25 years. It is bilateral in about 50 per cent of the cases, and the tumors are multiple in 33 per cent. Cystic lesions of the central nervous system, particularly the cerebellum, and of such viscera as the kidneys, pancreas, ovaries, and adrenal glands develop in about 25 per cent of the cases. Signs of central nervous system involvement, if present, are generally delayed until about 10 years after discovery of the ocular lesions. There is frequently a definite familial incidence of the disease.

The fundus picture is characteristic. A berry-like, reddish colored mass is seen in the retina, sharply demarcated from the surrounding area and supplied by an artery and a vein, both of which develop into wormlike enlarged stems carrying dark blood. Shiny white spots of exudate appear around the disc and macula. A globular retinal detachment subsequently develops and later may be followed by iridocyclitis, secondary glaucoma, cataract, and blindness. The angioblastoma is composed of thin-walled capillaries, glial tissue, and peculiar fat-laden cells between the vessels.

The treatment of angiomatosis is difficult, and success is possible only when the tumor can be destroyed in its early stage. Reports in the literature indicate that early angiomatous growths, whether in the eye or in other structures, respond to x-ray irradiation and diathermy. Unfortunately, the postirradiation observation

periods have been too short (the longest only three years) to warrant the drawing of any conclusions as to the duration of the derived benefit.

A case report is presented of a patient with angiomatosis retinae successfully treated with x-ray as determined by an 11 year follow-up examination. In 1941, this patient had an advanced lesion with retinal detachment in the right eye and an early lesion in the left eye. She was given a course of x-ray irradiation to each eye of 1,800 r. Two and a half years later, the right eye was unchanged, but the lesion in the left eye had become larger. An additional 2,000 r of x-ray irradiation was administered to the left eye, with resultant atrophy and scarring of the angioma, but no change in the dilated blood vessels leading to it. The patient then failed to return but was "rediscovered" in 1952. Examination at this time revealed the right eye to be amaurotic, with glaucoma and a mature cataract, but no congestion or pain. The left eye vision was 20/20. External and slit-lamp examinations were negative; there were no signs of lens opacification. The scarred angiomatous mass and its vessels were unchanged from their appearance in 1943, when last seen. A small new angioma, not present when the patient was seen in 1943, had developed in this eye. The results of this 11 year follow-up ,which was eight years longer than any previous postirradiation period on record, confirmed the previously recorded experience that treatment of angiomatosis retinae with x-ray irradiation is of no avail in advanced cases but may be successful in early cases. 20 references.—*Author's abstract.*

MISCELLANEOUS

45. *Recession Under Tenon's Capsule.* KENNETH C. SWAN AND THOMAS TALBOT, Portland, Oregon. Arch. Ophth. *51*:32–41, January 1954.

It is the purpose of this report to present a technic of handling Tenon's capsule which has been used at the University of Oregon Medical School since 1949. It has been directed toward maintaining the normal anatomy of Tenon's capsule and checking ligaments without detracting from the efficacy of the surgical procedure.

With the usual technics of recession and resection of the rectus muscle, Tenon's capsule is incised parallel to the limbus and at right angles to the muscle insertion. Most surgeons also incise Tenon's capsule alongside the muscle; thereby, a flap of Tenon's capsule is recessed or resected along with the muscle. This method of handling Tenon's capsule permits the conjunctiva to come in contact with the bare sclera to which it readily becomes adherent. Also, after Tenon's capsule is allowed to retract, it tends to roll up and form a cicatricial mass which may decrease mobility of the globe. Finally the check ligaments may be seriously altered. For these reasons, it seems desirable in resection and recession operations to preserve the normal relationships of Tenon's capsule. Also, it is desirable to place the conjunctival incision well away from the limbus to minimize postoperative irritation and cicatrization.

The above objectives have been achieved by placing the conjunctival incision behind the muscle insertion and parallel to the limbus. The conjunctiva is stripped

from Tenon's capsule by blunt dissection. Then, Tenon's capsule is incised in front of the muscle insertion but at right angles to the limbus. The incision is then extended over the muscle. When the edges of Tenon's capsule are retracted, the muscle is exposed within its capsule. The intermuscular membrane also is well exposed so that it can be buttonholed and incised cleanly alongside the muscle. After separation of the muscle capsule from Tenon's capsule, the muscle can be recessed and resected under Tenon's capsule without appreciably disturbing the check ligaments. In the closure, Tenon's capsule is approximated with one or two fine buried stitches. The conjunctiva is closed separately, and thereby its mobility is maintained. Postoperative reaction is minimal. Complications, such as scarring of the conjunctiva, granuloma formation, or retraction of the caruncle, have been less than when Tenon's capsule has been allowed to retract under the conjunctiva. 3 references. 8 figures.—*Author's abstract.*

BOOK REVIEW

Familial Nonreaging Food Allergy. COCA, Springfield, Ill., Charles C Thomas, 1953, 3rd edition.

Doctor Coca's third edition of *Familial Nonreaginic Food Allergy* is misleading because it is improperly titled. From a careful study of its contents and a conscientious attempt in the past year to use his technic in studying food sensitivity, I cannot agree with his observations in cases of known food allergies. The term allergy should be reserved for those conditions caused by union of antigen-antibody and resulting in an alteration from the normal of a specific tissue (shock organ) reaction.

I have no quarrel with his pulse-diet record and interpretation of the same. His normal ranges and limits may well be correct for the cases he studied, but they are not inclusive enough to cover the whole range of human norms and illnesses. Doctor Coca's inclusion of thirty-six symptoms as food allergies including fatigue, over-weight, diabetes, and stammering are those of an optimist's, especially when he includes cases of true atopic allergy such as bronchial asthma. Sympathectomy, in my opinion, is too drastic a procedure to resort to in cases of allergic diseases where the sympathetic nerves are secondarily involved, if at all, by the etiologic factors.

The entire book is extremely controversial from an allergist-internist point of view especially the chapters on cancer, multiple sclerosis, and idioblastic diseases of women. The studies on glaucoma are too few to be significant. The book is of no practical value for the clinician dealing with allergic diseases.—*F. Howard Westcott, M.D.*

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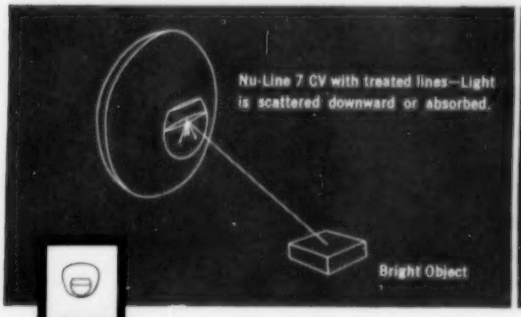

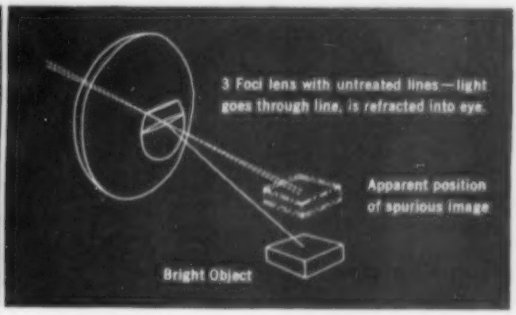
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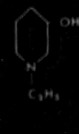
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